ENVIRONMENTAL TOBACCO STUDIES

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WORKPLACE

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ENVIRONMENTAL TOBACCO STUDIES

BIBLIOGRAPHY

A. **ETS Workplace Occupation**

1. Sterling, Thomas D., Does Smoking Kill Workers or Working Kill Smokers? Or, The Mutual Relationship Between Smoking, Occupation, And Respiration Disease. International Journal of Health Services, Volume 8, Number 3, 1978.

   -"Evidence accumulated since 1964 appears to show that occupation, not cigarette smoking, may be the primary cause of lung disease, especially of cancer and chronic obstructive disease." (p. 437)

   -"In analyzing the available evidence, we do not find support for claims that smoking is the major hazard to workers' lungs. Rather, it is the nature of their jobs that seems to cause their illness." (p. 443)

2. Carson, John R.; Erikson, Carol A. (USA), Results From Survey of Environmental Tobacco Smoke in Offices in Ottawa, Ontario. Environmental Technology Letters. Vol. 9 , June 1988.

   -"Based on the results of this survey, the average office worker was exposed to 0.0039 cigarette equivalent per hour (using nicotine as a marker) 0.0010 cigarette equivalent per hour (using UV-PM as a marker). Put another way, the time for exposure to one cigarette equivalent would have been 260 hours (using nicotine) or 1000 hours (using UV-PM)."(p.504)

3. Sterling, T., ETS Concentrations Under Different Conditions Of Ventilation And Smoking Regulation. Faculty of Applied Sciences, Simon Fraser University, Burnaby, B.C. S5A 1S6, Canada Proc. Indoor Amb. Qual. Conf. London, 1988.

   -"While smoking regulations are here to stay and will affect most offices under federal, provincial or municipal control in Canada, the haste to regulate smoking may have been based on the unrealistic modelled estimates of Repace and Lowrey or on "worst case" measurements in poorly ventilated workplaces, instead of on actual measurements of RSP levels in typical offices.

   The provision of a designated smoking area appears to effectively reduce ETS constituent levels in nonsmoking offices, even if the designated smoking area is not separately ventilated. However, we should caution that an exclusive reliance on regulating smoking while ignoring other sources of indoor pollution in the non-industrial work environment may accomplish little in meeting indoor air quality problems, especially in so-called "Sick Buildings"."
   (p. 97)

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4. Crawford, W.A., Health Effects of Passive Smoking in the Workplace. Proc. Indoor Amb. Air Qual. Conf. London, 1988.

-"If low levels of "passive smoking" increase the risk of lung cancer to a significant degree (as two studies seem to indicate), this strongly suggests that the dose-response curve is approximately logistic in shape, rather than in a straight line. If this is so for one chemical carcinogen (tobacco smoke) and one type of cancer, it is likely to be so for other chemical carcinogens and other types of cancer. This could radically alter present impressions of "tolerable levels of exposure" for a host of other agents." (p. 205)

-"The International Agency for Research in Cancer (10) 1986 reviewed the overall biological data and the epidemiological data and concluded:

> Examination of smoke from the different sources shows that all three types contain chemicals that are both carcinogenic and mutagenic. The amounts absorbed by passive smokers are, however, small, and effects are unlikely to be detectable unless exposure is substantial and very large numbers of people are observed. The observations on nonsmokers that have been made so far are compatible with either an increased risk from 'passive' smoking or an absence of risk. Knowledge of the nature of sidestream and mainstream smoke, of the materials absorbed during 'passive' smoking, and of the quantitative relationships between dose and effect that are commonly observed from exposure to carcinogens, however, leads to the conclusion that passive smoking gives rise to some risk of cancer." (p. 206)

-"That no atypical cellular changes have been found in the lungs of nonsmokers."

-"That nonsmokers do absorb one chemical peculiar to cigarette smoke - nicotine and this is measured as the metabolite cotinine."

-"There are competitors in the workplace for the induction of lung cancer."

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-"There are competitors for lung cancer in air pollution in industrialized countries."

-"There is no evidence of increase of lung cancer in nonsmokers during the decades of increasing prevalence of smoking."

-"There is inadequate data on the epidemiology of ETS in the workplace." (p. 208)

5. Sterling, T.D., Collett, Chris W., and Sterling Elia M., Environmental Tobacco Smoke and Indoor Air Quality in Modern Office Work Environments. School of Computing Science, Faculty of Applied Sciences, Simon Fraser University, Burnaby, British Columbia, Canada. J Occup Med (United States) January 1987, Volume 29 No. 1.

-"The effectiveness of such methods, as well as the overall relation of ETS to indoor air quality, are here evaluated, based on reviews of a large number of studies of indoor air quality in modern office buildings under normal use and occupancy. Under these conditions, ETS does not appear to contribute significantly to a build-up of contaminants in offices. Also, in two large series of studies of buildings with health and comfort complaints in the US and Canada, ETS does not appear to be associated with cases of building illness." (p. 57)

-"Under normal conditions of ventilation and occupancy, the concentration of pollutants appears to vary little between office areas where smoking is permitted and where it is not. For example, in 209 measurements of office buildings, median levels of CO were 3.1 ppm in smoking-permitted areas and 3.4 ppm in smoking-restricted areas. For all practical purposes, these are identical concentrations actually were found to be the same (0.038 mg/m3) for office areas where smoking was permitted and where it was restricted." (p. 59)

-"Designation of special smoking areas might remove multiple sources of irritation to smokers and nonsmokers alike. On the other hand, the segregation of smokers to specially designated smoking areas may have little effect and may well have undesirable impacts on ventilation performance. Concentrating smokers in designated smoking areas may place an excessive local burden on existing ventilation systems-a burden with which they may not have been designed to cope." (p.61)

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6. Sterling, T.D, Sterling, E.M., Environmental Tobacco Smoke. 1.2 Investigations on the Effect of Regulating Smoking on Levels of Indoor Pollution and on the Perception of Health and Comfort of Office Workers. European Journal of Respiratory Diseases 65 (Supplement 133), 1984.

-"A review of data from sealed, energy-efficient buildings (some investigated because of illness complaints) concludes that neither pollution levels nor patterns of symptoms differ between buildings with or without smoking restrictions. Trace amounts of aromatic hydrocarbons were found in many offices, but average levels of pollutants did not differ between buildings where smoking is permitted and where it is restricted. Also, no differences were found between the buildings associated with illness complaints and those that were not. It is noted that employees working where smoking is permitted reported substantially less strees than those where smoking is restricted, although there was a strong tendency for a high percentage of nonsmokers to rank building environment as poor in workplaces where smoking is permitted. Overall, health-related complaints were unrelated to workplace smoking regulations, and it is concluded that under conditions of inadequate ventilation, discomfort and illness result whether or not cigarette smoke is present. Symptoms decline dramatically (a 31 percent decline for eye irritation alone) whenever ventilation is increased and/or high ultraviolet emitting lamps are replaced."

7. Sterling, T.D., Sterling, E.M., Comparison of Non-Smokers' and Smokers' Perceptions of Environmental Conditions and Health and Comfort Symptoms in Office Environments With and Without Smoking. Ergonomics and Health in Modern Offices, Grandjean, I., Editor; Taylor and Francis, London, 11 references, 1984.

-"The relationships between physical stress, ergonomics, and health and comfort indices were not significantly different for the three groups with one exception: smokers had a greater tolerance for cigarette smoke than nonsmokers. No differences in the ventilation, temperature, humidity, lighting or odor were found with and without smoking. Employees working where smoking was permitted reported less stress than employees in non-smoking workplaces. The authors suggest that smoking does not affect the indoor pollution or health related building complaints."

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8. Simonato, L., Vineis, P., Fletcher, A.C., Estimates of the Proportion of Lung Cancer Attributable to Occupational Exposure. Carcinogenesis Vol.9 No.7, 1988.

-"From the studies reviewed it also appears that tobacco smoking has a very limited confounding effect. Various limitations of the exercise are discussed." (p. 1159)

-"Tobacco smoking does not appear to act consistently as a strong confounder of the association between lung cancer and elevated risks due to the exposure to carcinogens in the working environment." (p. 1164)

9. Sterling, T.D. and Mueller, B.; Concentrations of Nicotine, RSP, CO and CO2 in Nonsmoking Areas of Offices Ventilated by Air Recirculated from Smoking Designated Areas. AM. Ind. Hyg. Assoc. J., 1988.

-"Providing a designated but ~~not~~ separately ventilated smoking area appears to be effective in eliminating most components of ETS from nonsmoking office work areas." (p. 423)

-"Based on these findings, it is the authors' belief that the provision of a designated smoking area appears to be effective in eliminating most traces of ETS from the rest of the office space, even if the designated smoking area is not separately ventilated. An exclusive reliance on regulating smoking while ignoring all other problems besides smoking which may influence the quality of air in the nonindustrial work environment may accomplish little in addressing indoor air quality problems, however, especially in so-called "sick buildings." (p. 426)

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TRANSPORTATION

B. **ETS Transportation Issues**

1. Proctor, Christopher, A Study of the Atmosphere in London Underground Trains Before and After the Ban on Smoking. Toxicology Letters, 35 (1987).

   -"Measurements of the ambient atmosphere in London Underground train compartments were made before and after a ban on smoking. Levels of nicotine and carbon monoxide and estimates of airborne particulates are given. This paper describes the analytical techniques used in measuring constituents of tobacco smoke in the ambient air of public environments. Levels observed were all found to be far lower than recommended OSHA limits for safe exposure." (p. 131)

   -"Concentrations of nicotine in smoking compartments were found to vary between 16 and 74 ug/m3. The OSHA maximum threshold limit for 8-h industrial exposure to nicotine is 500 ug/m3 [1], so levels experienced in the Underground compartments were typically less than a tenth of this value.

   The values observed for airborne particles were similar to those likely to be found in a typical office or public house [6]. Values of carbon monoxide (about 3ppm) were found to be similar in smoking and non-smoking compartments. These levels were also far below the industrial threshold limit value (OSHA:50 ppm for 8-h exposure) and below that which would be experienced when sitting in a car in traffic [3]." (p. 133)

2. Holcomb, Larry C., Impact of Environmental Tobacco Smoke on Airline Cabin Air Quality. Environmental Technology Letters, Volume 9, 1988.

   -"A number of commercial airlines have moved recently, under pressure from government or on their own initiative, to ban smoking on at least some flights. Yet measurements of the constituents of environmental tobacco smoke ("ETS") fail to support claims that exposure levels in aircraft affect adversely the health of non-smoking passengers or crew. It appears, moreover, that the discomfort that can be caused by pollutants or environmental conditions aboard commercial aircraft often is misattributed to ETS because of ETS's visibility." (p. 509)

-Carbon Monoxide:

"...airline data reported by the National Academy of Science ("NAS") in the U.S. (14) and Lufthansa (10) note vlaues never exceeding 5.0 ppm. ...These concentrations were far below Frances's then 50 ppm maximum standard and the standards set by the Environmental Protection Agency ("EPA") and the Occupational Safety and Health Administration ("OSHA") in the United States." (p. 510)

-Particulate Matter:

"...a geometric mean ultraviolet particulate matter ("UV-PM") concentration in smoking sections of 34 ug/m3 and in non-smoking sections of 12 ug/m3. [These values are] well below EPA, OSHA nad international standards, particulate exposure at the levels noted above should pose no significant health threat."

-Nicotine:

"Such data show that smokers as well as non-smokers are exposed to minimal amounts of ETS, or at least to the nicotine component of ETS, on commercial aircraft with reasonably well operated ventilation system." (p.510)

-Other Significant Findings

"Other chemical substances not associated with or relevant to ETS are commonly found in studies of cabin air quality. Ozone has been associated with eye discomfort, chest pain or tightness, breathing difficulty, nasal irritation, persistent cough and sore throat.

"Low cabin humidity has been observed to contribute to dry, irritated eyes, especially in the case of contact lens wearers." (p. 511)

3. Duncan, D.B.; Greaney, P.P., Passive Smoking and Uptake of Carbon Monoxide in Flight Attendants. Journal of the American Medical Association 251(20), May 25, 1984.

-"Exposure to passive smoking during flights did not significantly alter carbon monoxide (CO) levels in expired air of commercial airline attendants."

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4. Oldaker, Guy B. III, Conrad, Fred C., Jr., Estimation of Effect of Environmental Tobacco Smoke on Air Quality within Passenger Cabins of Commercial Aircraft. Environmental Science Technology, Volume 21, No. 10, 1987.

-"The mean nicotine concentration for samples acquired in no-smoking sections was 5.5 ug/m3; in smoking sections of aircraft the mean nicotine concentration was 9.2 ug/m3. These concentrations correspond to estimated mean exposures of 0.0041 and 0.0082 cigarette equivalent per flight, respectively." (p. 994)

-"The results of this study shoe that (a) segregation significantly reduces the exposure of persons seated in no-smoking sections to ETS and (b) aircrafts' HVAC systems are primarily responsible for effection this reduction. In addition, the results indicate that average exposures to ETS are orders of magnitude less than exposures represented by smoking a single cigarette." (p. 998)

5. Oldaker, G.B. III; Correspondence (Comment on "Estimation of Effect of Environmental Tobacco Smoke on Air Quality within Passenger Cabins of Commercial Aircraft")

-"...the results of (our) study show that segregation significantly reduces the exposure of persons seated in no-smoking sections to ETS."

-"Empirical evidence is lacking in quantity and quality for a scientific evaluation of the quality of airliner cabin air or of the probable health effects of short or long exposure to it." (p. 1239)

6. Crawford, Allan W.; Environmental Tobacco Smoke in Airlines - Health Issues. Aerospace, July 1989.

-"The very high ventilation rates of 18-25 air changes per hour commercial aircraft effectively control all pollutions generated in commercial aircraft cabins. The provision of non-smoking and smoking sections meets the reasonable requirements of passengers.

The studies and reviews so far available do not lend support to the hypothesis that exposure to environmental tobacco smoke in aircraft may present a risk to the health of cabin staff or passengers. There are other factors which contribute to subjective complaints.

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On the grounds of health maintenance, there is inadequate scientific and medical research evidence to justify a banon smoking in airlines at present. Further research is required."

7. Jones, J.T., Letters to the Editor (Comment on Passive Smoking on Commercial Airline Flights), Journal of American Medical Association, Nov. 24, 1989. Vol 262, No. 20.

-Nicotine:

-"The mean quantity of nicotine reported, 12mg/m^3, amounts to only about 17 parts per billion-0.017 ppm"

-"Continuous exposure in the 4 hours of flight would total slightly less than 30 millionths of a gram."

-Propaganda:

-"The dry mouth, coughing, annoyance and other complaints cited are subjective and may owe more, I suggest, to the PAP (Princess and Pea) Factor than to actual smoke exposure, the subjects having been subjected, like all of us, to decades of scare propaganda."

Labriola, Daniel J., PEng, ND Technical Air Services Inc., Ibid.

-"I do not believe it is safe to interpret the environmental data, the urinary cotinine levels, or the health implications of these measurements as representing the typical level of passenger exposure. The subjective results are subject ot the same argument."

-"The report provides useful and needed data in the study of this serious public health risk. I suggest that further work be done to resolve the possible error sources before characterizing these pollutant levels and their potential health sequelae as typical for commercial airline travel."

9. Malmfors, Torbjrn, Thorburn, Daniel and Westlin, Arne. Air Quality in Passenger Cabins of DC-9 and MD-80 Aircraft. Environmental Technology Letters, Vol 10, pp. 613-628.

-"The air quality of passenger cabins of DC-9 and MD-80 aircraft has been studied on 48 representa-

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tive flights. A portable air sampling case was used. No observations of health effects were made. The average levels of the components related to environmentsl tobacco smoke, were respirable suspended particles 60, 250, 160 and 220 mg/m^3; and for carbon monoxide 0.6, 1.1, 0.8 and 1.1 ppm in Business Non-Smoking, Business Smoking, Tourist Non-Smoking and Tourist Smoking sections respectively The levels of carbon dioxide and relative humidity were about 1300 ppm and 25 percent in all sections respectively."

-"Although there are no standards for ETS in aircraft cabin air, comparisons with other official standards can be used to evaluate air quality in passenger cabins. The nicotine concentrations found are roughly one-tenth of the standard for the working environment, the carbon monoxide concentrations are about one-fourth of the standard for the working enviroment but slightly above what has been tentatively proposed."

HEART DISEASE

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C. Heart Disease

1. Helsing KJ; Sandler DP; Comstock GW; Chee E, Heart Disease Mortality in Nonsmokers Living with Smokers. Department of Epidemiology, Johns Hopkins University School of Hygiene and Public Health, Baltimore, MD. AM J Epidemiol (United States) May 1988, 127 (5).

- The relative risks for nonsmokers who lived with smokers were greatest among both men and women who were younger than age 45 in 1963, but the number of deaths in these groups was small, and confidence intervals were broad. We have very little data on other risk factors for arteriosclerotic heart disease in the study population.

  We have tried to adjust for some: smoking, by restricting the study to nonsmokers; age and sex, by assessing the risk separately for eight age-sex groups; and housing quality, marital status, and years of schooling, by binary variable multiple adjustment. Two other studies encourage us to disregard hypertension and cholesterol as possible confounding factors. However, other factors such as diet and exercise might differ in families with and without smokers; we cannot ignore the possibility that such differences could influence our findings.

*2. Kilpatrick, S. James, Effects of Passive Smoking on Ischemic Heart Disease: Mortality of Non-Smokers - A Prospective Study. American Journal Epidemiology, May 1985.

- Therefore, although a prospective study, the design is being used in an exploratory rather than a confirmatory manner, since no precisely specified hypotheses were enunciated prior to the beginning of the survey other than the vague reference to the exploration of risk factors in ischemic heart disease. Thus, for example, other analyses may have been conducted and not published because they did not reveal interesting conclusions which might be considered "significant". By its very nature, the analysis is partial. If the classification at entry into "never-smokers", "former smokers", "current smokers", is accepted then there is potentially, a three by three table for married women. We are only presented one row of this table. It would have been interesting to have seen the mortality of wives who are former smokers and wives who are current smokers, similarly classified against the reported status of their husbands.

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Other weaknesses in the study are the fact that 18% refused to participate. This is sufficient to bias the conclusions.

Finally, in the discussion section, the authors consider alternative explanations only to disregard them and then conclude that this association, if it exists, is of a causal nature; i.e., passive smoking increases risk of ischemic heart disease. Given that this is an exploratory prospective study with multiple endpoints, such a conclusion is unwarranted.

1. The choice of a one-sided test indicates that the authors are not neutral in this investigation of the effects of passive smoking.

2. Given that significant deviations in both directions are possible, the one-sided test, thus gives the appearance of more sensitivity than actually obtains, the conventional level of significance being 10% and 20%.

3. It is somewhat unconventional to use multiple levels of significance. When they are, they are usually set at 5%, meaning significant, and 1% meaning highly significant. Multiple levels of significance are appropriate in exploratory studies where the investigator is attempting to ascertain factors from a welter of potential factors.

   They adjust for age, systolic blood pressure, total plasma cholesterol, obesity index, and years of marriage even though their own analysis shows that there were no significant differences in systolic blood pressure, total plasma cholestrol, obesity index. Thus, they are including in the regression equation factors which in the discussion they put forward as not significantly different in the three groups (they cannot have it both ways).

*3. Witorsch, Philip, M.D., A Critique of Garland C. et al, Effects of Passive Smoking on Ischemic Heart Disease Mortality of Nonsmokers, A Prospective Study, American Journal Epidemiology, May 1985.

- There is no exposure verification. The authors instead rely on the husbands' self-reported smoking history. No data were obtained about duration of smoking, and number of cigarettes smoked per day was determined only for "current" smokers. There was no measurement of biologic markers of environmental tobacco smoke exposure.

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There was no date on how much smoking occurred in the home environment or other areas where the wives might have been exposed. The authors fail to demonstrate a dose response relationship.

The authors fail to demonstrate a dose response relationship. The number of cigarettes smoked per day is reported only for "current" smokers and this is unverified. There is, in fact, no statistically significant difference demonstrated in age adjusted death rates between the greater than 20 and the less than 20 cigarettes per day groups. There is no data on duration of smoking, an important component of any cumulative dose. There is, in fact, an inverse dose response relationship in the sense that the mortality is higher among wives of "former" smokers than among wives of "current" smokers if one looks at the age adjusted and crude death rates from ischemic heart disease in these two groups. This finding is inconsistent with the author's conclusion. In fact, one could conclude from such data that if a husband is a smoker, his termination of the habit places his wife at a greater risk of death from ischemic heart disease than if he continues to smoke!

The paper has a potential self-selection bias in that the subjects were volunteers who agreed to participate and answer the questionnaires. Furthermore, the 18% non-responders would be sufficient to alter the results, as pointed out by Dr. Kilpatrick in his accompanying critique.

While the authors address the factor of grief following upon the death of a spouse, emotional stresses that might have existed before prior to such an event are not addressed or taken into consideration, and these may be important relative to the development of and death from cardiovascular disease.

Ethnic variables, genetic factors, the existence of intrinsic disease such as diabetes, family history of cardiovascular disease, and other similar variables are not taken into account.

The authors also indicate that smoking exposure from previous marriages was not considered and state that this would have a generally conservative effect on the results. This may or may not be the case. For example, if women classified in the "never" group were previously married to smokers, they should be more properly classified in the "former" group.

It is also notable that the parameter that the authors use to assess the cardiovascular health effects of environmental tobacco smoke, mortality, seems rather insensitive. A more appropriate parameter would have been the incidence of heart attacks and angina in the subjects rather than mortality. It is somewhat surprising that such data is not reported. Perhaps it is available but does not support the author's contention that exposure to environmental tobacco smoke contributes to heart disease. The interpretation of the results and the conclusions as articulated by the authors, as well as their discussion, suggest a significant bias. For example, they cite the data in Table 3 to support the claim of a dose-response relationship between number of cigarettes smoked and death rate. However, the difference noted is not statistically significant.

Even though the authors qualify their claim of an association between fatal heart disease and exposure to smoking by stating that the data must be considered "provocative rather definitive", the claim that they make is still too bold and unjustified.

In summary, this study is poorly designed, the treatment of the data inadequate and inappropriate, and the results inconclusive. Furthermore, it would appear that the authors indulge a significant bias and distort the data to support a pre-conceived notion.

4. Schievelbein H; Richter F., The Influence of Passive Smoking on the Cardiovascular System. Preventive Medicine 13, November 1874.

- The conclusion can be drawn that neither CO nor nicotine is likely to play a role in the development and progression of coronary heart disease in those concentrations normally found in passive smokers.

- Cardiovascular effects of tobacco smoke have been studies in passive smokers far less extensively than in active smokers. Under real-life conditions, passive smokers inhale approximately 0.02 to 0.01 of the amount of particulate matter taken up by the active smokers. Their nicotine concentration in serum is within a range that is barely distinguishable from the background level. The increase in carboxyhemoglobin rarely exceeds 1%. In healthy subjects heavily exposed to tobacco smoke, no or only slightly acute effects on the cardiovascular system are found. Whether or not passive smoking is likely to aggravate symptoms in patients with advance coronary heart disease has not yet been unequivocally

established and requires further investigation. From a few studies on occupational groups exposed to carbon monoxide (CO) and from experiments with animals chronically treated with CO or nicotine, the conclusion can be drawn that neither CO nor nicotine is likely to play a role in the development and progression of coronary heart disease in those concentrations normally found in passive smokers.

- From a few studies on occupational groups exposed to carbon monoxide (CO) and from experiments with animals chronically treated with CO or nicotine, the conclusion can be drawn that neither CO nor nicotine is likely to play a role in the development and progression of coronary heart disease in those concentrations normally found in passive smokers.

There have been no experimental investigations into the acute effects of nicotine on the cardiovascular system in concentrations such as those found in passive smokers. If one extrapolates from the dose-effect relationship in smokers, no measurable acute effects of nicotine inhaled by passive smokers should be expected. Several animal experiments have been performed to study the chronic effects of nicotine. Their results, again, neither prove nor disprove an atherogenic effect of nicotine.

- In a few experimental studies, the influence of cigarette smoke on the cardiovascular system was measured directly. Although exposure in these studies was much higher than under real-life conditions, an increase in heart rate and blood pressure was either undetectable or only marginal. As shown in a study by Harke and Bleichert, the skin temperature, which decreases considerably while smoking one cigarette, remained constant.

- A number of studies have shown that under real-life conditions, passive smokers inhale only approximately 0.02 to 0.01 the amount of particulate matter taken up by active smokers. Carboxyhemoglobin increase in passive smokers under real-life conditions rarely exceeds 1%, while nicotine uptake is in the range where it can just be detected in blood stream. Nicotine levels up to 5 ng/ml obtained by gas chromatography should be interpreted with caution, because no zero level is found using this method even in subjects not exposed to tobacco smoke.

- From this finding it may be concluded that CO and nicotine uptake by passive smokers, under real-life conditions, do not exert an influence on the cardiovascular system or on metabolic processes.

- However, in light of the findings already discussed, and in view of the following facts, a causal relationship between cigarette smoking and CHD is much weaker than in male smokers. In the Framingham Study, no significant effect of smoking was observed among actively smoking women. If in female active smokers an effect of smoking on the development of CHD cannot convincingly be demonstrated, it is difficult to assume that such an effect is possible in female passive smokers.

- The incidence rate of CHD in pipe or cigar smokers is not, or is only slightly, elevated compared with nonsmokers despite the fact that in many pipe and cigar smokers a high uptake of carbon monoxide and nicotine can be found. Cigar and pipe smokers inhale tobacco smoke both actively, although much less than cigarette smokers, and passively. They may, in fact, be regarded as the group of passive smokers exposed to the highest concentrations of tobacco smoke.

- From the data available we conclude that passive smoking is not likely to have an effect on the development and progression of CHD. We conclude, therefore, that the 1983 Report of the Surgeon General on CHD is correct in making no reference to passive smoking as a possible cause. Our view also seems to conform with the prevailing scientific opinion as expressed thus far.

5. Ganh RC; Lincoln J., Effects of Passive Smoking in the Multiple Risk Factor Intervention Trial. American Journal of Epidemilogy.

- Based on the Multiple Risk Factor Intervention Trial data, Svendsen et al. (1) have reported a relative risk of 1.72 for death from any cause among male passive smokers (male nonsmokers married to a smoking wife vs. male nonsmoker married to a nonsmoking wife). This risk compares with a relative risk for male active smoking (male smokers vs. male nonsmokers) of 1.66, which we calculated from the Multiple Risk Factor Intervention Trial data (2).

  The effect measured by Svendesen et al. may be caused by stress rather than by passive exposure to cigarette smoke.

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5. Wald N.J.; Idle M.; Boreham J., Serum Cotinine Levels in Pipe Smokers: Evidence Against Nicotine as Cause of Coronary Heart Disease. The Lancet, October 10, 1981

- Large prospective studies have shown that pipe smokers have no material excess risk of coronary heart disease but cigarette smokers do, so that our observations indicate that nicotine is unlikely to be the major cause of the excess coronary heart disease mortality in cigarette smokers.

- The observation that pipe smoke have a relatively high nicotine intake but little if any excess risk of death from coronary heart disease strongly suggests that nicotine is not hte major cause of the excess risk found in cigarette smokers. Indeed it cannot be, unless nicotine absorbed through the pulmonary alveoli is more toxic than when absorbed through the buccal mucosa.

D. **Mutagenicity**

1. Husgafvel-Pursiainen K, Sister-Chromatid Exchange and Cell Proliferation in Cultured Lymphocytes of Passively and Actively Smoking Restaurant Personnel. Mutat Res March 1987.

   - Sister-chromatid exchange frequencies were measured in peripheral lymphocytes of 12 cigarette smokers, 20 passive smokers, and 14 non-smokers with no regular exposure to tobacco smoke. All active and passive smokers worked as waiters and waitresses in restaurants. The passive smokers showed neither an increased mean SCE value nor an increased number of high SCE frequency cells (HFCs) when compared to non-exposed non-smokers. However no significant correlation was observed between the individual mean SCE and the replication index.

     In this study, no significant increase was observed in the lymphocyte SCE level in the group of non-smokers with a long-term passive exposure to tobacco smoke. By examining 3 groups of individuals with different degrees of tobacco smoke exposure, this study did not find an influence of passive exposure on mean SCE level or number of HFCs in 20 waiters and waitresses.

2. Scherer G; Westphal K; Biber A; Hoepfner I; Adlkofer F, Urinary Mutagenicity After Controlled Exposure to Environmental Tobacco Smoke (ETS). Toxicol Lett (Netherlands) January 1987.

   - Twenty non-smokers on a defined diet low in polycyclic hydrocarbons (PAH) were exposed to environmental tobacco smoke (ETS) in an unventilated room for 8 h. The urinary mutagenicity in the 24-h urine samples as tested with the Salmonella (TA98) microsome assay did not significantly increase after exposure to either 10 ppm CO or 30-25 ppm Co. We conclude that exposure of non-smokers to ETS does not lead to an increase in their urinary mutagenicity, provided the exposure conditions are within a realistic range.

   - We conclude that exposure of non-smokers to ETS does not lead to an increase in their urinary mutagencity, provided the exposure conditions are within a realistic range.

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3. Mohtashamipur E; Muller G.; Norpoth K; Endrikat M; Stucker W Urinary Excretion of Mutagens in Passive Smokers. Institute of Hygiene and Occupational Medicne, University Medical Center, Essen University, F.R.G. Toxicol Lett (Netherlands) January 1987.

- Although clearly enhanced, no significant mutagenic activity could be found with 25ml equivalent urine/plate after passive exposure to cigarette smoke. The weak mutagenicities found were highly significant when 50ml equivalent urine/plate was tested. No direct correlation was observed between urine mutagenicity and the urinary cotinine concentration.

- Controversies are seen among the results of various authors (1-3), which do not permit a conclusion as to whether urine of passive smokers is mutagenic. Our results indicate that the inconsistency of the reports is possible due to some methodical difficulties of extraction and testing procedures and/or the experimental designs. Comparing the results of our mutagenicity assays with those of the cotinine in urine after passive exposure to cigarette smoke. Urinary excretion of mutagens depends on a variety of factors, the diet being one of them.

4. Sorsa, M.; Cytogenetic Effects of Tobacco Smoke Exposure Among Involuntary Smokers. Mutation Research, 222, 1989.

- Among passive smokers, in association with exposure to environmental tobacco smoke, no such induction of chromosomal damage has been documented. In the present paper we reported negative results on induction of chromosomal damage in 2 separate groups of intensive involuntary exposure to tobacco smoke, non-smoking restaurants personnel and newborn children of smoking mothers. While significant exposure in these groups is clearly seen in biochemical intake markers, e.g. cotinine and thiocyanate values in plasma, the conventional cytogenetic parameters, structural chromosome aberrations and sister-chromatid exchanges, are unable to detect the low exposures of involuntary smokers.

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- Only of the non-smoking mothers said in the personal interview that they had been exposed to ETS because of spouse's smoking. However, no significant increase of SCEs was detected in this group of passive smokers; the mean was 8.4 $\pm$ 1.0 as compared with 7.9 $\pm$ 0.9 of the non-exposed non-smoking mothers (n=18).

- The cytogenetic damage, well documented among active smokers (see e.g., IARC, 1986), cannot be shown to be associated with involuntary exposure to tobacco smoke in either of the two exposure situations studied, occupational or transplacental.

5. Maclure, Malcolm., Elevated Blood Levels of Carcinogens in Passive Smokers. American Journal of Public Health, October 1989, Vol. 79, No 10.

- Mantel concludes that the relative risk of passive smoking is too low to be detected by epidemiologic studies.

- If Mantel is right, assessment of the risk of passive smoking depends on measurement of the extent of absorption of carcinogens from tobacco smoke. No evidence has been reported to date of increased blood levels of a known carcinogen in passive smokers.

- Nevertheless, the magnitude of the elevation in adduct levels was small relative to normal background levels. Non-tobacco sources of 4ABP, and perhaps 3ABP, appear to exist. This was underscored by the fact that one woman with absolutely no passive exposure to tobacco smoke had levels of 4ABP-Hb higher than all the heavily exposed bartenders. Her level of 3ABP-Hb was undetectable, but another woman with minimal passive exposure had equally high 4ABP-Hb and the highest level of 3ABP-Hb in the study.

- Since our data are few, especially among confirmed passive smokers, and the assumption of linearity between adduct levels and risk is hypothetical, firm conclusions cannot be drawn.

- If studies like ours show that post-activation levels of other tobacco carcinogens are much lower in passive smokers than active smokers, it will add weight to the view that quantification of the risk of passive smoking is beyond the capability of questionnaire-based epidemiologic studies, except when the association between active smoking and disease is very strong.

- In conclusion, our results corroborate both the statement by the IARC that "passive smoking gives rise to some risk of cancer" and critics' contention that relative risks due to passive smoking may be undetectable.

E. Indoor Pollutants

1. Sterling E.M.; Collett C.W.; Kleven S.; Arundel A.; Typical Pollutant Concentrations in Public Buildings

- An archive of indoor pollutant levels in buildings under normal conditions of occupancy and operation has been assembled into a computerized Building Performance Database. This paper presents median values and ranges for pollutants, such as carbon dioxide, carbon monoxide, and formaldehyde, for which there are at least 20 data records.

2. Robertson G, Source, Nature and Symptomology of Indoor Air Pollutants.

- Without doubt, the pollutant most often blamed for these symptoms by the public is environmental tobacco smoke (ETS). However, there are usually confounding variables presented by a number of potential contaminants that precludes a quick analysis establishing a single source of contamination. The main problem being the incredible similarity between symptoms from widely different irritants or even environmental conditions. For example, identical symptoms have been reported for individuals exposed to formaldehyde, ammonia, oxides of nitrogen, and ozone. In addition, similar symptoms are reported by those individuals suffering allergic type reactions to numerous dusts and to microbial spores such as Aspergillus, Penicillium, and Cladosporium fungi, among others. Similar symptoms have been reported from exposure to cotton dust and fiberglass fragments and an ever increasing and similar problem is encountered due to low relative humidities. The latter is well known to frequent flyers of airliners where relative humidity levels are frequently as low as 10%, compared to a normal lower comfort level of say 40%.

- This similarity of symptoms is usually unappreciated by the public and in part it accounts for a bias against tobacco smoke, which happens to be the sole visible air pollutant. Furthermore, due to their unreliability, we, as a policy, refuse to rely upon or otherwise use the information generated by subjective building occupant questionnaires.

- Despite being the main suspect of the occupants in many of the buildings we have examined, we have determined high levels of environmental tobacco smoke to be immediate cause of indoor air problems in only four percent of the 223 major buildings investigated by ACVA between 1981 and 1987.

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- Significantly, in those few cases where high accumulations of ETS have been found, ACVA also has discovered an excess of fungi and bacteria in the HVAC system. these microogranisms usually are found to be the primary causes of the complaints and acute adverse health effects reported by building occupants.

- In general when one hears of a polluted building or a so-called "sick building", one hears familiar symptoms from occupants including eye and nose irritation fatigue, coughing, rhinitis, nausea, headaches, sore throats, and general respiratory problems. Without doubt, the pollutant most often blamed for these symptoms by the public is environmental tobacco smoke (ETS).

- As a result, we have made it our business to perform precisely such investigations. Despite being the main suspect of the occupants in many of the buildings we have examined, we have determined high levels of environmental tobacco smoke to be the immediate cause of indoor air problems in only four percent of the 223 major building investigated by ACVA between 1981 and 1987. This result has been corroborated. In a similar study of 203 buildings from 1978 to 1983, NIOSH found that only four of the buildings studied (two percent) had indoor air quality problems attributable to high concentrations of ETS. Significantly, in those few cases where high concentrations of ETS have been found, ACVA also has discovered an excess of fungi and bacteria in the HVAC system. These microorganisms usually are found to be the primary causes of the complaints and acute adverse health effects reported by building occupants.

- Perhaps the most serious problem of ventilation is that there is no effective legislation mandating the uniform use of minimum fresh air requirements. Certainly some authorities do specify ventilation rates at the design stage - most of these are based on ASHRAE or BOCA standards. However, the major problem is that there is no legislative structure, nor is there a practical policing methodology to ensure that the operators of buildings run their ventilation systems according to such designs.

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3. Crawford, W. Allan, On Air Pollution, Environmental Tobacco Smoke, Radon, and Lung Cancer. JAPCA 38, 1988.

- The general public is largely unaware of carcinogens in the environmental air, particularly indoors. The source most widely emphasised by health authorities in recent years is the exposure to environmental tobacco smoke. Robbins has cautiously suggested that the BaP contribution from ETS may be around 2 percent. What is not know to the general public is that BaP is commonly found in the emissions from the combustion of most fuels in transport systems, automobiles, whether gasoline or diesel fuled, oil fueled industry, now rarely coal-fired except for electricity producing power stations, the fireplace in the home, cooking and backyard burning.

- In one such calculation a person living in an urban area, 100 metres from an expressway with a 1 hour commute to a job in a central city location could inhale 20ng of BaP per day. If the worker had stayed at home the "dose" would have been 3ng.

- The USSG in his 1985 report "Smoking in the Workplace" scarcely mentions passive smoking. In relation to smoking and the workplace the USSG was subject to a strong adverse criticism by the AFL/CIO, the major trade union body in the USA. The AFL/CIO indicated that concentrating on the effects of smoking would seriously detract from efforts to clear the workplaces of numberous toxic hazards, would permit employers to blame smoking and exposure to ETS and would diminish efforts to recognise and control industrial exposures. The recent emphasis on ETS may similarly affect the vital steps to control the ambient air pollutions in urban, suburban and less populated areas as well as remote areas affected by fall-out.

4. Axelson O, Room for a Role for Radon in Lung Cancer Causation? Medical Hypothese, 1984.

- Passive smokers, taken as nonsmoking women married to smokers, seen to have an increased lung cancer risk, although these observations need further confirmation. it is remarkable, however, that the relative risk for passive smoking women is relatively high in comparison to the relative risk for active smoking women.

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The recent views on passive smoking should perhaps be supplemented by drawing attention to earlier observations of a familial factor in the etiology of lung cancer. Thus, relatives of lung cancer cases, but not spouses, were found to have some excess of lung cancer. The question is if this familial factor is of entirely genetic origin, however, or if it might represent an exposure in common to the relatives, namely to radon daughters in childhood and the earlier part of adult life. Furthermore, also behavioural habits might influence radon daughter exposure in homes, and smokers, as well as their family members, might have personality characteristics and interest giving preference to indoor activities to a relatively great extent. Hence, there might even be some uncontrolled confounding involved, when smoking is thought of as the major risk of lung cancer.

Not only changes in smoking habits but also other developments in the society need consideration with regard to the causes of lung cancer. By taking alterations in radon daughter exposure into account one might obtain a good supplementary explanation for the increasing lung cancer rates, especially as they seem to obtain also in nonsmokers.

5. Rylander, R., The Importance of Endotoxin and Glucan for Symptoms in Sick Buildings.

- Indoor mold growth seems to be a major cause of subjective symptoms. Investigations in the United States show that among 138 buildings with complaints or symptoms related to indoor air, 70% were buildings where microbial contamination, mainly fungi, was present (Robertson unpublished).

- Eye irritation in indoor air has previously been attributed to exposure to environmental tobacco smoke (ETS) (Weber 1984) and formaldehyde levels of exposure and in office buildings. In general, ETS does not seem to be an important agent for causing symptoms (Sterling and Sterling 1984). The amounts of other measured agents have also been low. In view of the data presented here, products from microbes are probably more important for the presence of eye irritation in indoor environments.

6. Crawford, W. Allan; Indoor Air Pollution and Environmental Tobacco Smoke. J. Roy Soc. Health, 1989.

- The prevalence and proportions of complaints of adverse effects and irritations has been described above from the U.K., U.S. and Canada, the U.S. and Canada data being government findings. Environmental tobacco smoke (ETS) exposure does not appear to be a major factor.

- There is an easy, but somewhat costly, solution - provide adequate ventilation. The costs will be recouped by more effective production and fewer days lost from minor illnesses resulting from the control of viruses, bacteria fungi and chemicals circulated, recirculated, accumulated and stored overnight in a shut down system for transmission the following day or after the weekend to produce a new form of Monday Morning Sickness.

- In the vast majority of studies of children and adults, on respiratory, cardiovascular and cancer problems, no account or scant account has been paid to the other environmental factors in the home and the workplace. They are listed by the U.S.N.R.C. Tobacco products, Marijuana, Clove cigarettes; Maternal smoking during pregnancy: Outdoor temperature, Humidity, Respirable and non-respirable particulates, e.g., fugitive dust, Pollens and other allergens; Crowding, Number and age of siblings, Total number of people/animals in dwelling unit, Total number of smokers in dwelling unit, House hold conditions, Frequency of air exchanges, Temperature and humidity, Use and conditions of air-conditioning units, Conditions of child care facilities, Unvented combustion products from heating/cooking stoves, Respirable and non-respirable particulates, such as wood smokes, Pollens, moulds, mites, Allergens and infectious organisms, Formaldehyde; Work/hobby related exposure to gases, fumes particulates; Annoyance response to tobacco smoking, only nicotine and its metabolites are specific to tobacco smoke. The other by-products can be produced by the combustion of other vegetable and organic biological matter and also by cooking.

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Witorsch, Philip; Health Effects of Indoor Air Pollution

- The available data suggest an association between spousal smoking and lung cancer risk in never-smoking women, but it remains to be established that marriage to a smoker is an appropriate surrogate for ETS exposure. Furthermore, it appears possible that the findings are the result of misclassification of study subjects. A limited number of reports purport to show an increased risk of cancer at sites other than the lung related to exposure to ETS. These data are subject to serious questions of biological plausibility and require confirmation before any meaningful conclusions can be reached. The available clinical, experimental, and epidemiological data do not support a relationship between ETS exposure and chronic respiratory disease, increased risk of development of atherosclerotic cardiovascular disease, precipitation of angina pectoris in patients with pre-existing ischemic heart disease, or other adverse cardiovascular effects, either at rest or during exercise.

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ANIMAL STUDIES

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F. Animal Studies

1. Matulionis DH, Effects of Cigarette Smoke Generated By Different Smoking Machines on Pulmonary Macrophages of Mice and Rats. J. Anal Toxicol Jul-Aug 1984.

   - The present study points out the need in research dealing with tobacco smoke inhalation for careful evaluation and monitoring of the smoke generation and delivery systems, as well as for awareness of inherent differences in biological responses to smoke among species.

2. Adlkofer F; Scherer G; Wenzel-Hartung R; Brune H; and Thomas C, Exposure of Hamsters and Rats to Sidestream Smoke of Cigarettes: Preliminary Results of a 90-Day Inhalation Study. Indoor Amb. Air Qual. Conf. London, 1988.

   1) It has been alleged that exposure to ETS may increase the lung cancer risk in non-smokers. Mainly three lines of evidence are cited in order to support this view: ETS contains carcinogenic and mutagenic compounds as shown by chemical analysis and in vitro assays, 2) epidemiolgical studies show a relative risk between 1 and 2 for non-smoking wives of smokers when compared to non-smoking wives of non-smokers, 3) an excess risk has to be assumed when extrapolating from smoking to passive smoking (2). On the other hand, the presently available scientific evidence for a causal relationship between passive smoking and lung cancer is very weak, if it exists at all (3). Animal inhalation studies could provide valuable information on the carcinogenic potential of inhaled ETS or SS of cigarettes in the respiratory tract.

   - No exposure-related changes in the clinicochemical and haematological parameters were observed. Histopathological examination of the respiratory tract by light microscopy revealed no differences between sidestream smoke exposed animals, sham-exposed animals and untreated cage controls. Despite the absence of changes visible in the light microscope, it was decided to look at a small number of samples of trachea and lung parenchyma by electron microscopy. This investigation revealed suggestive evidence of slight changes in exposed animals which reversed for the most part or completely during the 90 days following the end of exposure.

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One of the aims of this pilot subchronic inhalation experiment, was to detect early lesions (if any) which could be induced by an unrealistically high, but tolerable sidstream smoke exposure dose in rats and hamsters. The exposure level chosen was a particle mass concentration of about 4mg/m^3 which parallels several recent long-term diesel exhaust inhalation studies (13). This concentration us up to 100 times higher than the smoking-related particle levels reported for real-life situations (1). The nicotine uptake by the smoke-exposed animals, as indicated by serum nicotine and cotinine concentrations, is also between one and two orders of magnitude higher than that found in humans passively exposed to tobacco smoke.

- No treatment-related changes were found in the respiratory tract by light microscopy. Limited evidence derived from e.m. studies on a small number of samples suggested that exposure damaged ciliated cells in the trachea and lung parenchymal cells, but these effects disappeared during 90 days following the end of exposure. The most obvious of these changes were an increase in the number of alveolar macrophages, the occurrence of pigmented macrophages in the lung parenchyma and partial deciliation of tracheal epithelial cells. Rats exposed to diesel exhaust at a concentration of 6.3 mg/m^3, 8 h/d for 5 days or longer are reported not to have cleared the diesel particles from the lungs 90 days after the end of the exposure (14). It is assumed that the particle load of the lungs is the main cause of the induction of lung tumors in diesel exhaust-exposed rats (13).

- The outcome of this subchronic inhalation study suggests that the particle burden of the lung of rodents exposed to sidestream smoke is much less than that in diesel-exposed animals. From our results we further conclude that the application of this exposure regime in a long-term study with hamsters and rats is feasible. On the other had, an exposure does of 4 mg/m^3 might lead to some alterations of the mucociliary escalator. It is extremely unlikely that these lesions are caused by passive smoking in humans under real-life situations since prolonged exposure to such high levels of sidestream smoke does not occur. In this context it is noteworthy that deciliation is rare in non-smokers (15).

ACUTE EFFECTS

G. Acute Effects

1. Hugod C.; Hawkins L.H.; Astrup P., Exposure of Passive Smokers to Tobacco Smoke Constituents. Int. Arch. Occup. Environ. Health, 1978.

- In contrast to the opinion that acrolein is the most important irritating agent in tobacco smoke, exposure to acrolein appears to be only slightly irritating. Even as it is indisputable that passive smoking is connected with immediate discomfort that may be accentuated considerably by the concomitant presence of bronchitis, sinuitis, conjunctivitis, etc. it is difficult to document or to render probable that passive smoking under usual conditions should have a lasting adverse health effect on otherwise healthy individuals.

- An adverse health effect of passive smoking in grownup individuals would not be expected if only regarding the inhaled amounts of those tobacco smoke constituents that through the years have been considered pathogenic: nicotine, HCN, TMP and CO. The CET values for nicotine and HCN are negligible and can be disregarded. For CO and nitrogen oxides there is no reason to assume that these components are inhaled by passive smokers in such amounts that they should be considered pathogenic. However, a rise in COHb to approximately 3%, which is most unlikely obtained from passive smoking, will decrease the threshold for intermittent claudication and angina pectoris in patients with obliterating arterial disease.

- The CET-value for TPM is so high (about 11) that the passive smoker will never inhale more than what equals 1/2-1 cigarette per day. In our opinion and apart from the exceptions mentioned, no data exist to document that any of the gasphase or particulate phase constituents of tobacco smoke reviewed in this study have a lasting adverse health effect in otherwise healthy individuals subjected to passive smoking.

2. Comstock G.W.; Meyer M.B. Helsing K.J.; Tockman M.S. Respiratory Effects of Household Exposures to Tobacco Smoke and Gas Cooking. Am Rev Respir Dis 1981.

- But the extent to which smoking by others or cooking with gas are detrimental to human health is a question that is still unsettled, largely because of the difficulties in measuring individual exposures and because of inconsistent findings.

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The records of 1,724 residents of Washington County, Maryland, who had participated in 2 studies of respiratory symptoms and ventilatory function were analyzed to evaluate the effects of exposures at home to tobacco smoke generated by other members of their households and to fumes from the use of gas as a cooking fuel. The presence of a smoker in the household other than the subject was not associated with the frequency of respiratory symptoms, and only suggestively associated with evidence of impaired ventilatory function. The use of gas for cooking was related to an increased frequency of respiratory symptoms and impaired ventilatory function among men, being most marked among men who have never smoked. There was no evidence that cooking with gas was harmful to women.

The frequency of major respiratory symptoms among subjects showed little evidence of an association with the presence of some one else in the household who smoked cigarettes. This held true regardless of sex or smoking history of the subjects.

3. Shephard R.J.; Collins R.; Silverman F., Responses of Exercising Subjects to Acute Passive Cigarette Smoke Exposure. Environmental Research, 1979.

- Responses to 2 hr of "passive" cigarette smoke exposure have been tested in 23 healthy young men and women who were performing intermittent bicycle ergometer work sufficient to increase respiratory minute volumes by a factor of 2.5

- The main complaints were of odor and eye irritation. Cough, nasal discharge or stuffiness, and throat irritation were also reported, but wheezing shortness of breath, and tightness in the chest were both uncommon and unsupported by objective evidence of brochonspasm. A small increase of tidal volume and respiratory minute volume seemed due to anxiety rather than airway irritation. Static lung volumes were unchanged.

- Static lung volumes show no consistent reaction to cigarette smoke exposure. However, the 4 + 3 cigarette experiments suggest a small decrement of dynamic lung volumes consistent with a small and practically unimportant decrease of airway conductance, while the 6 + 3 cigarette exposures induce statistically insignificant trends in the same direction.

4. Shephard R.J.; Ponsford E.; Basu P.K., Effect of Cigarette Smoke on the Eyes and Airway. Int. Arch. Occup. Environ. Health 43, 1979.

- Two limitations of the present study must be stressed - smoke concentrations were not measured, and our conclusions were drawn from responses to a forced-choice multiple response questionnaire. Since non-smokers often report annoyance from what prove to be very low concentrations of cigarette smoke, it could be argued that their symptoms are 'suggested' by a slight odor of the offending smoke. The fact that lachrymation and stinging of the eyes were reported almost equally by ex-smokers and continuing smokers argues strongly against such a conclusion. Nevertheless, it is possible that by conducting the survey in ophthalmological offices, we did concentrate on a group of subjects who were more likely to complain about their vision. It would thus be worthwhile repeating observations on a randomly selected population.

5. Hartmann A; Weber A; Danuser B., Passive Smoking. Acute Effects on the Lung Function of Sensitive Persons. Institute for Hygiene and Arbeitsphysiologie, Dermatologische Universitatsklinik, Zurich. Soz Praventivmed (Switzerland) 1987.

- From the relationship between the degree of air pollution due to tobacco and its acute effects on healthy persons it is possible to estimate the still tolerable level of air pollution for healthy adults. The results and conclusions of the studies published by now on acute effects of passive smoking on patients with bronchial asthma are partially contradictory and do not allow a reliable estimation of the upper limit of tobacco smoke exposure for this particularly sensitive group.

6. Bruenkreff B; Fischer P; Remijn B.; van der Lende R; Schouten J; Quanjer P., Indoor Air Pollution and its Effect on Pulmonary Function of Adult Non-Smoking Women: III. Passive Smoking and Pulmonary Function. Int J Epi Demiol June 1985.

- The association between pulmonary function and exposure to tobacco smoke in the home was investigated in a sample of adult, non-smoking women living in a rural area. The women were all participants in a large longitudinal survey on the natural history and determinants of chronic non-specific lung disease. On cross-sectional analysis, several pulmonary function parameters were found to be significantly associated with exposure to tobacco smoke in the home.

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There was no association between exposure and pulmonary function decline.

Weber A., Environmental Tobacco Smoke. 3.4 Acute Effects of Environmental Tobacco Smoke. European Journal of Respiratory Diseases 65 (Supplement 133), 1984.

- Hence, it follows that there is a relationship between air pollution due to ETS (measured by the parameters CO, nicotine and PM) and the reported annoyance and eye irritation. Thus, the observed effects can be explained, at least to some extent, by ETS. However, this relationship in only applicable if mean values of large groups are considered. In fact, if we take each room into consideration and calculate the individual correlations between the mean pollutant concentrations of each room and the reported effects in this room, we obtain a very poor relationship.

  The data demonstrate that from the measured CO values in an individual room, one cannot easily draw conclusions on the extent of individual irritation and annoyance due to ETS. Therefore CO can only be used as an indicator to evaluate the degree of some gaseous components due to ETS and to estimate roughly the acute effects on a large sample of persons. In field studies, individual psychological factors (relationship with smoking co-workers, general job satisfaction, attitude towards smoking) may considerably influence the individual evaluation of irritation and annoyance.

8. Lebowitz M.D., The Effects of Environmental Tobacco Smoke Exposure and Gas Stoves on Daily Peak Flow Rates in Asthmatic and Non-Asthmatic Families. European Journal of Respiratory Disease 65 (Supplement 133), 1984.

- Environmental tobacco smoke (ETS) showed no effect on daily peak flows (Vmax) or symptoms in children or adults, asthmatics, or others in a study of 117 families (229 subjects) in Tucson. Monitoring was conducted over a 2-year period, using daily diaries for symptom information and peak flows, measured daily with a flow meter. Indoor carbon monoxide was significantly associated with gas stove usage, but not with ETS, gas furnaces, or other gas appliances. Children exposed to ETS had a nonsignificantly higher average Vmax, but Vmax was negatively affected in adult smokers and ex-smokers. Indoor total suspended particulates (TSP) had an effect on daily symptoms in adults and on Vmax in asthmatics that must be associated with characteristics of indoor TSP not correlated with ETS.

- Some of the same respiratory diseases may occur in indoor situations in which high levels of respiratory particles and gases are due to wood burning, not ETS.

- Schilling et al. utilizing indoor measurements showed that indoor levels of respirable particles were higher in homes with smokers, but that there was no effect on children's symptoms or lung function. Also, Lebowitz et al. influences in body size and lung function eliminated the influences of parental smoking on children's lung function.

- There were no effects of ETS on Vmax or symptoms in children or adults, asthmatics or others.

  Indoor TSP did, however, have an effect on adult's daily symptoms and on asthmatics' Vmax, which must be associated with other characteristics of the indoor TSP (the part not correlated with ETS).

  Unfortunately, because of sample size and the number of confounding factors, precise exposure-effect could not be determined. This would appear to be a major methodological problem for these types of studies, as one must account for co-variables (age, sex smoking), symptoms (asthma, allergy, AOD), indoor and outdoor meterological, pollutant and pollen differences.

9. Kentner M; Triebig G; Weltle D., The Influence of Passive Smoking on Pulmonary Function--A Study of 1,351 Office Workers. Prev Med Nov 1984.

   - Until now it has been difficult to ascertain how much passive inhalation of tobacco smoke affects bronchopulmonary function. To answer this question, an investigation involving 1,351 white collar workers was carried out. Passive smokers evaluated by this method showed essentially no decrease in parameters describing ventilatory function. It is concluded from the dose and time-effect relationships obtained in active smokers between the lung function parameters and the duration of tobacco smoke exposure on the one hand and the daily consumption of cigarettes on the other, that passive smoking in small doses may have no essential effect on pulmonary function.

- Taking our own results into consideration, it seems that the passive inhalation of tobacco smoke at home or in the work place by healthy individuals probably does not lead to any essential impairment of pulmonary function. To what extent this also applies to extreme passive exposure to smoke must remain the subject of further investigation. Thus, for example, persons working in restaurants or in poorly ventilated rooms may be exposed to high levels of smoke pollution.

10. Adlkofer F; Scherer G; Weimann H, Small Airways Dysfunction in Passive Smokers. New England Journal of Medicine, 307(7), Aug. 14, 1980.

- White and Froeb state in the March 27 issue that they found differences in mid-expiratory and end-expiratory flow (FEF 25-75% and FEF 75-85%) in their comparison of nonsmokers with passive smokers and smokers. This statement is remarkable since not all investigators who have used FEF 25-75% have been able to distinguish between smokers and nonsmokers, because only a limited number of smokers had abnormal test results.

  Is is possible that passive smoking and smoking 40 cigarettes or more per day impair pulmonary function by nearly the same percentage? These findings are difficult to believe and require further investigation.

  The methods used by White and Froeb are open to criticism. Of course, FEF 25-75% and FEF 75-87% have proved to be more sensitive than forced vital capacity and forced expiratory volume in one second (FEV) in the ability to show dysfunction of the small air ways. However, since the coefficient of variation for FEF 25-75% is three times larger than those for FVC and FEV, there is some doubt about whether the evidence of FEF 25-75% and FEF 75-85% is more conclusive than that of FVC and FEV.

  The authors must have been faced with another difficult problem - the selection and grouping of the subjects. The information provided does not exclude the possibility of bias.

11. Shephard, R.J.; Collins, R.; Silverman, F.; "Passive" Exposure of Asthmatic Subjects to Cigarette Smoke. Environmental Research 20, 1979.

- Fourteen asthmatic subjects volunteered for a controlled trial of 2-hr passive exposure to cigarette smoke. Our data thus do not suggest that asthmatic subjects have an unusual sensitivity to cigarette smoke.

- Findings included some increase of heart rate and respiratory minute volume, probably of emotional origin, a tendency of increase in functional residual capacity and residual volume in some experiments, and small decreases of dynamic lung volumes. The asthmatic subjects also showed emotional reactions to the cigarette smoke, including the tachycardia, and possibly the preexposure increase of FRC and TLC. Taking the group as a whole, there was no evidence of impairment of dynamic lung volumes during the passive cigarette exposure. It might be argued that emotional reactions to the smoke-filled chamber were sufficient to mask such a response. However, we did not form the impression that subjects were unduly alarmed by the experiment, and the observed tachycardia after 2-hr passive smoke exposure was slight.

  Although several of the asthmatic subjects claimed wheezing and tightness in the chest would result from passive exposure to cigarette smoke, the physiological data give little support to the concept of a subgroup with particular sensitivity. On the experimental day, the group claiming sensitivity showed a tendency of increase in static lung volumes, and a decrease in dynamic volumes. However, changes were of almost equal magnitude during the sham exposure. We may thus hypothesize that the observed reactions are due to the suggestibility of the subjects rather than a pharmacological or allergic reaction to cigarette smoke. In support of this view, the only significant difference in the "sensitive" group was a greater FEV relative to the corresponding time in the control exposure, presumably due to greater sympathetic activation and/or arousal in the smoke-filled environment.

- While there may be valid grounds for controlling the cigarette smoke concentration in "public" air (Shephard et al. 1979a), the present data offer little support to the view that asthmatic subjects need special consideration in this regard. Complaints of tightness in the chest and wheezing were more frequent than in the general population, but the only statistically significant physiological response was a very small decrease of TLC. Further, this change was not significantly greater in those complaining of chest symptoms. The subjective reactions thus seems but one more manifestation of annoyance, almost universal at the concentration evaluated.

- It is conceivable that more clear-cut physiological reactions might have been engendered at higher smoke concentrations. Nevertheless, the value used is the highest likely figure to which an asthmatic subject will be exposed (Sebben et al., 1977), and indeed with adequate ventilation smoke concentrations can be held to substantially lower figures.

- We would thus conclude that the specific sensitivity of asthmatic subjects is not a major consideration when determining air quality criteria for rooms contaminated by cigarette smoke.

12. Kentner, M. & Weltle, D.; Passive Tobacco Smoke Inhalation and Lung Function in Adults. Proc. Indoor Amb. Air Qual. Conf. London, 1988.

- To find an answer to the question, whether passive inhalation of tobacco smoke may cause a reduction of lung function, an investigation involving 1,364 white collar workers with healthy lungs was carried out. Ex-smokers and passive smokers showed no flow reductions, which were out of the range of the normal variability. From this it follows that average everyday passive smoke exposure in the office or at home does not lead to essential impairments of lung function in healthy adults.

- Some studies demonstrate a significant negative effect of parental smoking other results are inconsistent and a number of investigations fail to find any associations between parental smoking habits and a decreased pulmonary function in their children. These inconsistencies may depend on misclassification bias, socioeconomic status, outdoor air quality, home heating, air conditioning and humidity, genetic factors and in utero or lactational mechanisms by maternal smoking.

- Up to now eight studies have been published on passive smoking and lung function in healthy adults. These are exclusively cross-section studies.

- Only in two studies the flow-volume curves. Whilst Brunnekreef et al. found a statistically significant reduction of PEF and MEF 75 in PS in comparison to NS, Schilling et al. were unable to establish such a relationship for any lung function parameter.

- From the findings available so far there is no evidence that average everyday passive smoke exposure in the office or at home leads to an essential reduction of lung function in healthy adults.

- Under unfavourable conditions (forced and passive smoke exposure over many years, small rooms, heavy physical work, prior illnesses of the respiratory system) a reduction in lung function due to passive smoking might be possible, particularly in women.

13. U.S. Department of Health and Human Services, Report of Workshp on Respiratory Effects of Involuntary Smoke Exposure: Epidemiologic Studies. May 1-3, 1983.

- The relatively small differences in the effects found in the various studies discussed at this workshop may be real and represent true differences among the various communities studied in the measurable effect of involuntary smoke exposure. Such differences may be caused by regional and geographic variations in levels of indoor air pollution that migh result from differences in housing - (e.g., predominantly indoor living versus predominatly outdoor living.) On the other hand, the differences may also be due to methodologic differences in data collection an/or analysis and in the way in which potentially confounding variables have been handled.

- The difficulty of controlling for potentially confounding variables was recognized. Such variables include: 1) unvented combustion products from different kinds of stoves used for both heating and cooking, e.g., gas, wood and kerosene, 2) other indoor pollutants such as formaldahyde and resirable particulate matte, 3) indoor pollutants of organic origin such as polles, molds, mites, other allergens and infectious organisms, 4) characteristics of indoor environments such as temperature, humidity, and frequency of air exchanges, 5) socio-economic status, culture (ethnic), and such factors as crowding, number of siblings, household conditions, child care, reporting biases, etc.

6) demographic and medical characteristics of the study poulation such as age, sex martial status, the presence of underlying respiratory conditions, atopy, infections, disability an/or co-morbidity,) parental symptoms such as productive cough which will affect reporting, 8) maternal smoking during preganancy, 9) annoyance responses and other psychological or social responses to tobacco smoking in a nonsmoker. Extensive as this list of potentially compounding variables may be, the importance of taking them into consideration in the study design and analysis cannot be overemphasized.

- A review of the data from the studiws which have been carried out or are in progress which address the effect of passive smoking on the respiratory system suggests that the effect varies from neglibible to quite small. From this review, ti was not possible to deteremine whether there is a specific group which is at increased risk or what the mechanism of the effect (if any) may be. The data sets which already exist and are presently being collected are large and complex and, not surprisingly, there are differences, although small, in the results, among the data sets discussed at this workshop. These differences may be due to real differences among the populations being studied or may be due to methodologic differences that inevitably occur from study to study, both in the data collection and analysis. A common approach to the analysis may help to answer this question. It seems likely that the existing data sets contain sufficient information to allow some conclusions to be reached on the effect of passive smoking on the respiratory system. New large scale population studies (of subjects above 5 years of age) should probably not be initiated until the existing data have been thoroughly evaluated. There is, however, an urgent need for the development and evaluation of non-invasive biological markers of exposure.

K. Nicotine/Cotinine

1. Balter NJ; Eatough EJ; Schwartz SL, Application of Physiological Pharmacokinetic Modeling to the Design of Human Exposure Studies With Environmental Tobacco Smoke

- The predominance of nicotine in the ETS gas phase implies that nicotine is not a satisfactory marker for the particle phase and, perhaps, not for whole ETS pre se. In this respect a group of compounds unique to environmental tobacco smoke appear to act as conservative tracers of the particulate portion of environmental tobacco smoke, i.e., they appear in indoor air from no sources other than environmental tobacco smoke, and changes in their concentration in particles. Examples of these conservative tracers are pyridine, 3-ethenylpyridine and particulate phase nicotine and solanensol.

- The first issue is whether the nicotine exposure of an individual exposed to ETS follows the exposure of the individual to other components of ETS. Unless it can be demonstrated that changes in the behavior of nicotine in air with time parallel those of other components, especially those that may be associated with the toxicity of ETS, then biomarker studies of nicotine or cotinine will reflect only nicotine exposure, and cannot be used as a bais for extrapolation to ETS per se.

- The combined results of the various studies reported to date suggest that gas phase nicotine for total nicotine may not be a good marker of the particulate phase of environmental tobacco smoke due to its rapid removal from indoor environments.

- The atmospheric and pharmacokinetic data presented here are not that encouraging with respect to nicotine as a surrogate. The foregoing discussion quite clearly demonstrates the uncertainties associated with the relationships of atmospheric nicotine concentrations to ETS. Furthermore, even allowing for the reservations directed at nicotine as an ETS surrogate, there is considerable question about the means for estimating nicotine exposure. Physiological pharmacokinetic modeling reveals that much more detailed work is necessary before cotinine can be anything more than a semi-quantitative measure of nicotine exposure. Though data presently available suggest that several compounds, including 3-ethenylpyridine, pyridine, and particulate phase nicotine and solanesol, may be good tracers for environmental tobacco smoke these compounds have not yet been used in extensive studies to determine their feasibility as tracers for environmental tobacco smoke.

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2. Jarvis MJ, Uptake of Environmental Tobacco Smoke. Addiction Research Unit, Institue of Psychiartry, Denmark Hill, London, UK. IARC Sci Publ (France) 1987.

- But the short half-life of nicotine in the body means that it is best suited to quantifying exposure over a period of a few hours only. Estimating the magnitude of the passive smoking dose is difficult, and it is of doubtful validity to extrapolate from the uptake of one cigarette-equivalent of carbon monoxide is absorbed, the dose of a cigarette-equivalent. It seems unlikely that nonsmokers could absorb more than one or two mg of nicotine in a day, even if they spend the majority of their waking hours in heavily smoke-polluted atmospheres. Comparison of cotinine concentrations in urban nonsmokers and active smokers suggests that average nonsmokers may receive a dose of about 0.2mg of nicotine per day. But future progress in understandihng will be best assured if epidemiological methods and biological monitoring of exposure markers are combined in the same studies.

3. Muramatsu M; Umemura S; Fukui J; Arai T; Kira S, Estimation of Personal Exposure to Ambient Nicotine in Daily Environment. Environ Res Oct 1984.

- To evaluate the actual exposure level of nonsmokers to environmental tobacco smoke (ETS) in their daily life, the exposure level of ambient nicotine was measured with a nicotine personal monitor carried by nonsmoker. Average exposure levels of nicotine, even in such smoky places as cars, coffee shops and pubs, were less than 45 micrograms/m3. As a result of all-day monitoring, the highest amount of nicotine inhaled in a day was estimated, in this study, to be up to 310 micrograms, equivalent to actively smoking 0.31 ordinary cigarettes.

- Thus, the nicotine level in daily environments will rarely exceed 100ug/m3. If a man stays in a room with a 100ug/m3 nicotine level for 1h, the amount of nicotine he will inhale is estimated only to be equivalent to that inhaled by actively smoking about 0.05 cigarettes.

Therefore, we can say that the amount of nicotine inhaled by a nonsmoker in his daily life is far smaller than that inhaled by a smoker through active smoking.

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4. Muramatsu M; Umemurs S; Okada T; Tomita H, Estimation of Personal Exposure to Tobacco Smoke with a Newly Developed Nicotine Personal Monitor. Environ Res Oct 1984.

   - To evaluate the actual level of exposure of nonsmokers to tobacco smoke in their living environments, a convenient personal monitor of nicotine specific for tobacco smoke has been developed. The amounts of nicotine inhaled by passive smoking in various living environments were estimated to be in the range of 0.9-40 micrograms/hr. These levels are equivalent to those from the active smoking of about 0.001-0.04 ordinary cigarettes in 1 hr.

5. Biber A; Scherer G; Hoepfnew I; Adlkofer F; Heller WD; Haddow JE; Knight Gj, Determination of Nicotine and Cotinine in Human Serum and Urine; An Interlaboratory Study. Forschungslaboratorium, Prof. Schievelbein, Munich F.R.G. Toxicol Lett (Netherlands) Jan 1987.

   - An interlaboratory study aimed at determining nicotine and cotinine in human serum and urine was carried out. The ratios of urinary cotinine concentrations between active and passive smokers differed widely from laboratory to laboratory. The reasons for this are not yet known and necessitate further investigation.

6. Letzel H; Fischer-Brandies A; Johnson LC; uberla K; Biber A, Measuring Problems in Estimating the Exposure to Passive Smoking Using the Excretion of Cotinine. Toxicol Lett (Netherlands Jan 1987)

   - Quality control studies on cotinine measurements following low level environmental tobacco smoke (ETS) exposure are rare. The exposure to ETS was controlled and systematically changed in a series of experiments in a climatic chamber. Our data show that estimating low-level ETS exposure by measuring urinary cotinine is highly susceptible to uncontrolled variation and errors. Sufficiently reliable estimates of low-level ETS exposure can be made only when fractionated sampling over 48-72 h is used and when the urine samples are kept frozen just after collection.

7. Adlkofer F; Scherer G; Vonhees U, Passive Smoking. New England Journal of Medicine, Vol. 312. No. 11, 1985.

   - In our own study of 193 smokers we found a level of 1.11ug per milligram of creatinine- similar to that obtained by other workers but almost eight times lower than the figure of 8.57 given by Matsuskura et al. Similarly, the level of 0.68 that they reported for nonsmokers under normal living conditions is an order of magnitude higher than the figures obtained by other authors.

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- This discrepancy is too large to be explained by difference between the Japanese and Westerners in nicotine intake or in urinary creatinine concentrations, and it suggests strongly that radiommunoassay used by the authors may not have been specific enought for cotinine, so that because of immunologic cross-reactions, substances related and not related to smoking were measured in addition to cotinine.

9. Schepers Georg, Walk Rudiger-Alexander, Cotinine Determination by Immunoassays May Be Influenced by Other Nicotine Metabolites. Arch Toxicol, 1988.

- Polyclonal rabbit anticotinine antiserum, which can be used for biomonitoring nicotine uptake by the determination of cotinine in body fluids, was checked by a competitive ELISA for its cross-reactivity with nine nicotine metabolites.

- Therefore it is possible that cotinine determinations performed by immunochemical methods - especially in urine - may yield overestimated cotinine concentrations.

10. Sepkovic Daniel W., Haley Nancy J., Elimination From the Body of Tobacco Products by Smokers and Passive Smokers. JAMA, Aug 15, 1986 vol 256, No. 7.

- The slower clearance in nonsmokers of a terminal nicotine metabolite commonly used to measure exposure to tobacco smoke could result in a misinterpretation of "cigarette equivalents" which some researchers use to calculate passive exposure. The prolonged elimination of cotinine shown by passive smokers precludes a direct extrapolation to "cigarette equivalents of smoke uptake" from a single measurement of urinary cotinine.

- Cautious interpretation of these data is called for since the cotinine concentrations in smokers are many times greater than those in passive inhalers. It is apparent that components present in concentrations more than 100 times greater, although eliminated more quickly, are likely to be of greater health consequence than compounds present in very low concentraions some hours longer.

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Children Studies

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N. Children Studies

1. Pershagen, Goran, Childhood cancer and malignancies other than lung cancer related to passive smoking. Mutation Research, 222 (1989) 129-135.

-"The available epidemiological data provide no conclusive evidence of an effect of maternal smoking during pregnancy on the risk of cancer in children. Only a few studies have been performed on ETS and cancer risks in adults, except for lung cancer, and no firm conclusions can be based on the results."

-"The epidemiological evidence is not consistent regarding an effect of fetal exposure to maternal smoking during pregnancy on the risk of cancer in children."

-"Only a few studies have been performed on exposure to ETS and the risk of malignancies other than lung cancer in adults. It is not possible to draw any firm conclusions from these studies."

2. Ownby, Dennis R. and McCullough, Judith, Passive exposure to cigarette smoke does not increase allergic sensitization in children. From the Division of Pediatric Allergy-Immunology, Henry Ford Hospital, Detroit, Mich.

-"The purpose of this study was to learn whether children passively exposed to parental cigarette smoke would be more frequently sensitized to common allergens or would have higher concentrations of allergen-specific IgE."

-"Children of smoking mothers had significantly greater IgD concentrations ($p=0.03$) and were more likely to be referred for allergy evaluation ($p=0.0001$), but these children did not have increased concentrations of total or allergen-specific IgE. Exposed children were not more likely to be serologically sensitive to any of the allergens tested. We conclude that children passively exposed to cigarette smoke do not produce more IgE to common allergens nor are they more likely to produce IgE to any particular allergen."

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3. Haggart, Monica and Giblin, Michael, Passive Smoking and Colic-Like Behavior in Babies. Health Visitor, 1988 Vol 61

-"Eighty infants were included in a study to examine a possible connection between a colic-like syndrome in young babies and atmospheric tobacco smoke. Although previous research had suggested that such a connection was very likely, the study found no evidence for this. Various other factors were examined, but no connections were found. This unexpected finding is discussed and possible alternatives are suggested."

4. Bert Brundereef, Douglas Docker, Frank Speizer, James Ware, John Spengler, Benjamin Ferris. Home Dampness and Respiratory Morbidity in Children. Am. Rev. of Respiratory Disease, Nov. 1987.

-"The relationship between home dampness and pulmonary functio was weak, with an estimated mean reduction of 1.0% om FEF associated with dampness and 1.6% with molds. We conclude that dampness in the home is common in many areas of the United States and that home dampness is a strong predictor o symptoms of respiratory and other illness symptoms among 8- to 12-yr old children."

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O. Misclassification, Confounding Variables, Validation of Exposure

1. Lee Peter N., Misclassification of Smoking Habits and Passive Smoking: A Review of the Evidence. International Archives of Occupational and Environmental Health Supplement 1988.

   - How accurate are statements about smoking habits? This book presents the results of a comprehensive review in which the literature on the subject is newly interpreted. It is shown that smokers are misclassified as non-smokers in epidemiological studies often enough to explain completely the increased lung cancer risk seen in self-reported non-smokers in relation to their spouse's smoking habits. This study overturns the commonly held view that increased risk is a consequence of exposure to environmental tobacco smoke and highlights the difficulty of making valid inferences from epidemiological data.

2. Vandenbroucke JP, Passive Smoking and Lung Cancer: A Publication Bias? Department of Clinical Epidemiology, University Hospital, Leiden, The Netherlands. British Medical Journal (Clin Res) (England) Feb 6 1988, 296 (6619).

   - To assess the likelihood of publication bias in a recent review of the effect of passive smoking on lung cancer the evidence from the reviewed papers was visualized on a "funnel" plot. The resulting plot was compatible with a publication bias but only in studies on men. Further studies of passive smoking and lung cancer in men seem to be warranted.

   - The mechanism of such a bias can be imagined. Given the near unanimity in medical circles about the risk of active smoking, epidemiologists will have difficulty in exonerating the smoking habit from causing harm. Confronted with weak data on men alongside stronger data on women, authors or reviewers might be inclined to drop the former in favour of the latter. Theoretically two possible remedies for this unsatisfactory situation exist: either call for a new and large study on men only or invite researchers to submit their unpublished low power studies to accumulate their hidden information.

3. Darby S.C. & Pike M.C., Lung Cancer and Passive Smoking: Predicted Effects from a Mathematical Model for Cigarette

- Epidemiological studies of active smokers have shown that the duration of smoking has a much greater effect on lung cancer risk than the amount smoked. This observation suggests that passive smoking might be much more harmful than would be predicted from measures of the level of exposure alone, as it is often of very long duration frequently beginning in early childhood. In this paper we have investigated this incidence of lung cancer among smokers, ex-smokers and non-smokers in a cohort of male British doctors. Contrary to our expectation the model predicted only a slight increase in relative risk with increasing duration of passive exposure. Allowing for exposures early in life does not therefore explain the discrepancy between exposure indicated by cotinine measurements in those passively exposed.

  It is clear that epidemiological studies of passive smoking are particularly obtaining adequate histories of such past exposure and because the studies need to avoid even slight biases as the relative risks involved are small.

- Although the risk is greater if exposure occurs both in childhood and in adult life than if it occurs in only one of the two periods, the drastic increase in risk with increasing duration of exposure, seen in active smokers, is absent. For example, exposure at the rate of one cigarette per day from birth to age 65 incurs only a 21% greater relative risk than exposure at the rate of one cigarette per day from age 20 to age 65 (1.77 compared with 1.45). Direct analogy with the effect of duration of smoking as seen in active smokers of around 20 cigarettes per day would have predicted nearly a four-fold increase.

  The relative risks associated with exposures in the range one tenth to one cigarette per day are less than two, and are thus smaller than the underlying background risk of lung cancer due to causes other than cigarettes.

  We conclude, however, that the relative risks of lung cancer due to passive smoking as estimated by Wald et al. (1986) seem to be at variance with the number of cigarettes per day equivalent estimated from cotinine measurements. This discrepancy remains even when allowance is made, within the framework of our model for the fact that passive smoking may commence in early childhood, and when the parameters of the model are estimated allowing the British doctors' themselves to have been exposed to passive smoking.

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4. Pron Ge; Burch JD; Howe GR; Miller AB, The Reliability of Passive Smoking Histories Reported in a Case-Control Study of Lung Cancer. American Journal Epidemiol (United States) Feb 1988, 127 (2).

- A test-retest design has been used to examine the reliability of passive smoking histories in personal interviews.

  Quantitative measures of exposure to passive smoke, i.e., number and duration of exposure, were even less reliably reported. Nonsmoking respondents gave the most reliable information. The low reliability of self-reported duration of exposure to passive smoke is consistent with the inability of several studies to detect a significant dose-response relation with lung cancer risk when measures of dose that depend solely on duration are used.

  There are a number of possible reasons for these inconsistent results. The use of smoking by a spouse as the only index of passive smoke exposure could lead to a substantial misclassification bias if subjects are exposed at work or at home from household members other than their spouses. The use of hospital controls in case-control studies can be a major source of bias for studies of active smoking, and if passive smoke exposure is associated with diseases that lead to hospitalization, studies of passive smoking would also be biased. Finally, there is the possibility that subjects may provide unreliable information on their passive smoke exposure, since this is obviously a more difficult exposure to measure than that of active smoking.

- To our knowledge, this is the first study to assess the reliability of information reported on passive smoke exposures in personal interviews. Test-retest estimates of reliability suggest that misclassification of such exposures may be extensive.

  Quantitative measures of exposure to passive smoke, i.e., number and duration of exposures, were even less reliably reported.

  It is relevant that reliability is a measure of repeatability and not validity, and even if results were completely reliable, there would be no guarantee against misclassification bias in epidemiologic studies.

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The low reliability of durations of exposure to passive smoke reported in this study suggests that it would be difficult to detect significant dose-response relations with measures of dose that depend solely on duration.

The unreliability of duration measures of dose used in this study, e.g., years lived with a person who smoked, suggests that other measures of dose should be employed for the study of exposures to passive smoke.

5. Letzel H., E. Blumner and Uberla K., Meta-Analyses on Passive Smoking and Lung Cancer Effects of Study Selection and Misclassification of Exposure. Environmental Technology Letters, Vol. 9, 1988.

- Meta-analyses of studies on lung cancer and passive smoking both by WALD and the authors have shown greater differences in the pooled relative risk. In our paper three scenarios with conservation rates of misclassification are assumed and their effect on individual and pooled relative risks are examined. All the results of 27 meta-analyses are not statistically different from unity with the exception of 4 results, 3 of which are occurring if one selects only 4 case control studies with minor quality. Considering 10 case control studies alone 24 out of 1,023 possible meta-analyses are technically significant. These are dominated by 3 studies of lower quality. Our results lead to the conclusion that based on meta-analyses with proper correction for misclassification the null hypothesis has to be further accepted.

  As with other statistical methods, the results of a meta-analysis are only valid if certain requirements are fulfilled. The two most important problems are:

  If studies with "negative results" are omitted - the most frequent reason being that such studies are often unpublished - the real false-positive error probability may greatly exceed the calculated value. The other basic problem is the quality of the individual studies. The questionable results from studies with a poor design will not lead to a valid meta-analysis with scientifically convincing results.

- One can argue differently as to how the Hirayama study should be adjusted and whether the Tiochopoulos study should be accepted for inclusion in a meta-analysis at all. Depending on these decisions one comes up with meta-analyses which do or do not include unity within the 95% confidence interval of the pooled relative risk estimate.

- We preferred a more direct approach and considered the misclassification bias for the exposure under the conditions of the case-control studies. We also included very moderate assumptions about correct classifications of the disease. Unless histologically proven, a tumor of the lung might be anything from a metastasis of a non-pulmonary primary tumor to a primary sarcoma. Therefore we assumed a 5% false-positive error probability for the diagnosis lung cancer in studies without scientific histology.

  Taking all this evidence together, our calculations show that the findings of all studies about female lung cancer from passive smoking are consistent with the null-hypothesis. Their results can just as well be explained in terms of bias. Some of these studies have been heavily criticized for insufficient methods. It is doubtful which studies should be included in a meta-analysis on passive smoking and lung cancer. Therefore we calculated all logically possible combinations of the 10 case-control studies in females and found that only 2.3 % gave lower confidence limits above 1.0 under the assumptions of scenario C. In all of these "significant" combinations there was a domination by studies of questionable quality.

  This brings us to the final conclusion that there are presently only 2 alternatives - accepting the null-hypothesis or creating new empirical evidence by performing a really good study.

6. Lee PN, An Alternative Explanation for the Increased Risk of Lung Cancer in Nonsmokers Married to Smokers, 1988.

   - The Independent Scientific Committee on Smoking and Health (ISCSH) recently concluded that environmental tobacco smoke (ETS) exposure increases lung cancer risk among non-smokers by 10-30 percent. Since non-smokers have very low exposure to smoke constituents such a large effect seems implausible. Detailed evaluation of the available evidence indicates the increased risk of lung cancer seen in epidemiological studies of non-smokers is due to bias and not ETS.

   - There appears to be a huge discrepancy, of 2 or even 3 orders of magnitude between the claimed relative effects of passive and active smoke exposure and the much smaller relative exposure of passive and active smokers.

If the epidemiology is to be accepted as valid, an explanation would have to be sought either in a greater toxicity of ETS than mainstream smoke or in a greater susceptibility of non-smokers. While sidestream smoke has higher concentrations of some toxic chemicals than mainstream smoke, the relevance of this finding to environmental tobacco smoke which is aged, vastly diluted, chemically altered sidestream smoke, is not at all clear. There does not appear to be any direct evidence that ETS is particularly noxious. Nor is there any direct evidence that active smoking reduces susceptibility to relevant effects of ETS.

- While such explanations cannot be completely ruled out, the obvious alternative explanation - that the epidemiology is in some way biased - seems on the face of it much more plausible. Though the claimed effect of passive smoking may be large when viewed against the magnitude of effect predicted on dosimetric grounds, it is actually quite small when viewed against the magnitude of effect it has in the past proved possible to reliably identify using epidemiological methods.

It has been suggested that a well designed case-control study should be able to confirm a two-fold difference in risk but that, for differences less than this, the power of the study design may be inadequate. In trying to assess whether bias might have arisen in the epidemiological evidence it is necessary to consider potential limitations of the available data.

Confounding. Not all the studies considered have taken into account the possible confounding effect of factors know or suspected to be related to lung cancer, such as occupation or nutrition.

Inappropriate choice of controls. General scientific principles demand that like should be compared with like as far as possible. In a number of studies, there were clear exceptions to this. While inappropriate choice of controls may have materially biased some studies, it is probably not the main explanation for the huge discrepancy.

Non-reporting bias. One problem in combining results from various studies to come to an overall assessment of the evidence, by so-called "meta-analysis" is the possibility that the studies being combined are not representative of all those that have been carried out. One can easily imagine an investigator running a range of statistical analyses, finding a few significant associations of interest, and then publishing papers on those, ignoring the non-significant relationships.

Lack of objective measure of ETS exposure. A limitation of all the published epidemiological evidence is lack of objective measurement of exposure to ETS. While it can be shown that marriage to a smoker is indeed associated with increased levels of cotinine, the relatively crude method used for determining exposure leads to the possibility of bias in case-control studies where knowledge of disease may consciously or subconsciously affect reporting of ETS exposure.

Schwartz SL; Balter NJ (USA), ETS--Lung Cancer Epidemiology:Supportability of Misclassification and Risk Assumptions. Environmental Technology Letters. Vol 9 No 6, June 1988.

- The NAS Committee on Passive Smoking used epidemiologic data to estimate the risk of lung cancer associated with ETS exposure. Mathematical models were used to assess the influence of smoking - and exposure-status misclassification. These models and the database for their application are thoroughly examined. For smoking status misclassification, the model is technically sound; for exposure misclassification, the model is empirically logical, but mathematically can require very precise data. Further effort is necessary to compensate for the paucity of data to which the models can be applied.

8. Kilpatrick SJ Jr., Misclassification of Environmental Tobacco Smoke Exposure; Its Potential Influence on Studies of Environmental Tobacco Smoke and Lung Cancer. Medical College of Virginia, Virginia Commonwealth University Richmond VA. Toxicol Lett (Netherlands) Jan 1987, 35 (1).

- The effects of selection, confounding, misclassification and bias must be eliminated from case-control studies of 'passive smoking' and lung cancer before a meaningful interpretation can be made. Misclassification includes the misclassification of the subject's non-smoking status, of the disease status

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or of the spouse's smoking habits. This paper shows that inflation of the amount smoked by the husbands of female lung cancer cases may have accounted for the apparent 'dose-response' relationships in 3 widely referenced case-control studies.

- That misclassification exists in these studies is now widely accepted. In general, respondents are more likely to falsely inflate exposure if the case dies of cancer than of some other disease. There is indirect evidence for the presence and effect of differential misIcassification of exposure to ETS. For example, Garfinkel et al. show that the effect of ETS exposure at home is null (an odds ratio of 1) when the case or her husband is the respondent; however, this null result is converted into an odds ratio of 3 when the son or daughter is the respondent.

- The most recent case-control study of ETS and lung cancer, one which went to some pains to verify exposure classification, provided evidence suggesting a case misclassification rate of exposure as high as 25%. This figure may be compared to the 21% overall case misclassification rate required to produce the results in the 3 studies under review.

- In summary, when a spouse's smoking status is used to estimate a non-smoker's ETS exposure, 'a considerable amount of misclassification' may result. Since selection bias and confounding must also be considered, extreme caution is required in the interpretation of these studies. This is especially so when the literature as a whole contains several studies reporting no significant association between ETS exposure and lung cancer, as well as various inconsistencies, both among and within studies.

9. Lee PN, Lung Cancer and Passive Smoking: Association of an Artefact Due to Misclassification of Smoking Habits? Toxicol Lett (Netherlands) Jan 1987, 35 (1).

- 1,775 subjects were asked about their current use of tobacco products or nicotine chewing gum. 1,537 provided a sample of saliva for cotinine analysis. Of 808 who claimed not to be users of such products, 20 (2.5%) had cotinine values above 30ng/ml, suggesting their self-reports were false. In another study, 540 subjects were interviewed on two occasions. 10% of subjects claiming on one occasion never to have smoked made inconsistent statements on the other occasion. A third study showed a strong tendency for smokers to marry smokers. Bias caused by misclassification of smoking habits coupled with between-spouse smoking habit concordance can completely explain reported apparent excesses in lung cancer risk in non-smokers married to smokers.

- It is concluded that most or all of the apparently increased risk of lung cancer in self-reported non-smoking women married to smokers is attributable to bias.

10. Letzel HW; Johnson LC, The Extent of Passive Smoking in the Federal Republic of Germany. Prev Med Nov 1984, 13 (6).

- A representative survey of 1,670 persons between 14 and 65 years of age was conducted in order to obtain current data on active and passive smoking in the Federal Republic of Germany. It consistently compares with our preliminary definition of passive smoking. A reconstruction of Hirayama's definition reveals parallel results in terms of maximum exposure time when compared with our preliminary definition. A direct comparison between both definitions showed inconsistencies to an extent that could jeopardize the results of a case-control study. Data demonstrate a massive effect of measuring techniques on study results with regard to the frequency and extent of passive smoking. They also show the vulnerability of the calculation of equivalence of actively smoked cigarettes.

- In our opinion, this shows that there is a huge gap between theories of equivalents and actual exposure. We simply cannot yet estimate the carcinogenic potency of an exposure.

  A major deficiency of previous epidemiologic studies is their crude way of estimating exposure. Our data suggest that the techniques used may be inadequate.

  The relevance of future epidemiologic studies depends not only on adequate study designs, but also, primarily, on reliable and valid methods for estimating exposure.

  Thus far, we do not know of any study that has convincingly demonstrated a cause-effect relationship between passive smoking and lung cancer. This is primarily due to the lack of a validated assessment technique.

11. Pittenger D.J., Passive Smoking (Letter). New England Journal of Medicine 312 (11), March 14, 1985.

- Procedural, statistical, and conceptual flaws found in an earlier study on passive smoking that limit interpretation of the data and conclusions of the research discussed. The correlation of 0.15 found between the number of cigarettes smoked and urinary cotinine levels indicates that 97.75 percent of the

variation in continine levels was the result of error or other contributing factors that were not assessed. Information on how subjects were solicited or whether randomizing techniques were used was not included. No mention was made concerning the matching of groups for medical history, socioeconomic status, occupation, or other health related variable. It is suggested that urinary cotinine analyses in a group of nonsmokers totally isolated from all forms of smoke would have demonstrated the radioimmunoassay technique's validity.

12. Pershagen G., Validity of Questionnaire Data on Smoking and Other Exposures, With Special Reference to Environmental Tobacco Smoke. Eur. J. Respir. Dis. (Denmark) 1984.

- Information on several types of exposures is needed in epidemiological studies on health effects due to environmental tobacco smoke (ETS). Perhaps the single most important factor is to get accurate information on smoking habits of the subject under study. For instance, the findings of increased lung cancer risks among non-smoking women, married to smokers may be invalidated if some of these women actually smoked and if this was more common than among women in the comparison group. The same reasoning may be used for respiratory symptoms in children; is there a bias in the reporting of smoking habits for children to smokers in comparison with similar data for children to non-smokers? Finally, a brief evaluation will be made of questionnaire information on occupational exposures and other factors which may be of importance as confounders in a study of health effects due to ETS.

- It should be noted that no data are available on the validity of smoke exposure information obtained in a study on effects of ETS. In a study design where health effects of ETS from smoking habits of the respondents are investigated one may well imagine systematic errors in the reporting of smoking habits. The quality of this type of exposure information should be a topic for future research.

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13. Lee PN, Passive Smoking and Lung Cancer Association; A Result of Bias? Independent Consultant in Statistics and Epidemiology, Sutton, Surrey, UK. Hum Toxicol (England) Nov 1987, 6 (6).

- 5 Estimates of bias based on these data indicate that misclassification can explain the unexpectedly high lung cancer risk associated with spouse smoking in epidemiological studies of self-reported never smokers.

- There now seems to be a consensus that the overall data (which relates mainly to female non-smokers) indicate a positive association, with the average RR variously estimated at 1.30, 1.41, 1.2-1.5 or 1.35. Although this association is statistically significant, it is by no means clear that it represents a causal effect of exposure. When viewed against the very low exposure to smoke constituents from passive smoking, the magnitude of this association is statistically significant, it is by no means clear that it represents a causal effect of exposure. When viewed against the very low exposure to smoke constituents from passive smoking the magnitude of this association is surprisingly large and it is necessary to consider the possibility that it might have arisen to a great extent as a result of bias.

- It has been estimated on this basis for the US that passive smokers have 0.02% of the exposure of active smokers for men and 0.01% for women. Using linear extrapolation, these figures would provide relative risk estimates of 1.002 and 1.001 , two orders of magnitude lower than those observed in epdiemiological studies. Robins also calculated that non-smokers take in the equivalent of an extremely small number of cigarettes per day in terms of respriable particulates. He further points out the higher cigarette equivalent numbers which can be calculated for the nitrosamine NDMA are likely to be very misleading since NDMA is in the vapour phase and is water soluble and, with shallow inhalation, will be dissolved in the mucous membranes before it can reach the lungs. He notes too that estimates based on cotinine may also give a misleadingly high indication of relative lung exposure of passive and active smoker since nicotine, which is also water soluble, is present mainly in the vapour phase in environmental tobacco smoke, whereas it is mainly in the particulate phase in mainstream smoke.

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- Taking into account the available information, it seems more reasonable to conclude that exposure to smoke constituents of non-smokers is too low to explain the moderate increase in risk of lung cancer seen in epidemiological studies in self-reported never smokers married to smokers. This increase in risk is much more plausibly explained by misclassification of smokers as non-smokers that by a direct effect of passive smoking.

14. Lee PN, Misclassification as a Factor in Passive Smoking Risk (Letter). Lancet Oct 11 1986, 2 (8511).

- If misclassification of smokers as non-smokers and other possible biases are not taken into account the result is likely to be an estimate of lung cancer deaths attributed to passive smoking that is incompatible with the amounts of smoke which non-smokers are exposed.

15. Friedman GD; Petitti DB; Bawol Rd, Prevalence and Correlates of Passive Smoking. Am J Public Health, Apr 1983, 73 (4).

- The duration per week of exposure to others' tobacco smoke in different locations was tabulated from the questionnaire responses of 37,881 non-smokers and ex-smokers who received multiphasic health checkups in 1979 and 1980.

  Although the reported passive smoking of married persons was strongly related to their spouses' habits, categorization by spouses' smoking resulted in considerable misclassification.

- In the absence of direct measurements of smoke exposure, which are impractical for large population studies, questioning the subjects would appear to be the best approach for assessing their own passive exposure. As suggested by some of the spouse data in this study, our questionnaire is far from ideal. Nevertheless, there was a weak positive correlation of exposure duration with physiologic effects of smoking, particularly SCN levels, suggesting both that this questionnaire does provide an assessment of passive smoking that has some validity and that passive smoking involves physiologically measurable degrees of smoke exposure in non-smokers. We recommend that further effort be devoted to improving methods for assessing passive smoking by questionnaire.

Q. General Reviews of ETS/General Critiques of Poor Studies

1. Consumer Report, The Murky Hazards of Secondhand Smoke. Consumer Reports 50:1985.

- But if the Japanese findings are correct, the heaviest exposures to tobacco smoke tend to occur in the home. Even nonsmokers working with more than six smokers in the same room did not exhibit the highest recorded cotinine level unless they also got a hefty does of smoke at home. Why should the home be such a significant source of exposure even though the workplace may harbor more smokers per square foot? Often the primary reason is ventilation. According to a 1980 report in the journal Science, a complete exchange of indoor and outdoor air may occur only once or twice an hour in a private dwelling, about the same rate as for the worst ventilated commercial premises. At the opposite extreme is the modern airliner, where a complete air change takes place roughly every three minutes. Most commercial structures rank somewhere in between, with the best ones clocking air changes each five or six minutes. Thus a lone smoker in the kitchen might create a thicker haze than would several co-workers smoking on the job.

- In short, the NCI's findings suggest that the average person could smoke two cigarettes a day without measurably increasing mortality risk above that of a nonsmoker. The word "measurably," though is important. Essentially, the NCI's conclusions suggest that passively inhaling the equivalent of one to two cigarettes a day will generally not produce any effects on mortality large enough to detect.

- Within a few months, however, a large-scale study by the American Cancer Society, a longtime crusader against smoking, produced very different results. Lawrence Garfinkel, of the society's Department of Epidemiology and Statistics, reported the findings in the June 1981 issue of the Journal of the National Cancer Institute.

  Comparing lung-cancer rates experienced in a population of 176,739 non-smoking women in the U.S., Garfinkel found no significant difference between the wives of smokers and nonsmokers. "Nonsmokers married to smoking husbands," he reported, "showed very little, if any increased risk of lung cancer."

- One Hong Kong study found that nonsmoking wives of smokers had a lower rate of lung cancer than their smoke-free counterparts, which suggest, if nothing else, that the time to retire the spouse index may be at hand.

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2. Schamahl Dietrich F.K., AP Interview: Lung Cancer Due to Passive Smoking?, No -- All Just Speculation! Artzliche Praxis, Vol. 40, No. 92, 1988.

- A critical examination of the epidemiological data yields no indication of an increased risk of lung cancer due to passive smoking, and such a risk also appears extremely unlikely from the aspect of toxicology. This is the opinion of Professor Dietrich F. K. Schmahl, executive director of the Toxicology and Chemotherapy Institute of the German Cancer Research Center in Heidelberg, in an AP interview with Kirk Rohwedder.

- The epidemiological data available to date are controversial. The studies that demonstrate a risk are so seriously questioned by reputable epidemiologists that for me, as a nonepidemiologist, these data provide no reason to believe that an elevated risk of cancer exists. And from the toxicological aspect, to which I can contribute something, an elevated risk appears to be extremely unlikely.

- Prohibitions are political decisions. There is no scientific justification for such prohibitions as far as the risk of lung cancer due to passive smoking is concerned. I believe that the nonsmoker has a certain right not to be bothered by smokers. But the increased risk of lung cancer is not a sound link in the line of reasoning, and thus is not to be taken seriously. If health politicians want to pass prohibitions, that's their business -- but they cannot cite a definite risk of cancer connected with the matter of passive smoking as we are discussing it.

3. Lebowitz MD, The Potential Association of Lung Cancer with Passive Smoking. Division of Respiratory Sciences, University of Arizona College of Medicine, Tucson, Arizona. Environmental International, Vol 12, 1986.

- The epidemiological studies conducted so far on the effects of involuntary smoking of spouses indicate the major difficulties of calculating good estimates of risk. Ascertainment biases, incomplete data acquisition, incomplete conformation of morbidity and/or mortality, and failure to account for the many co-linear risk variables seem to diminish risk estimates obtained from those studies. The American and Scottish studies appear to have been able to handle these problems more completely, and they were not able to reject the null hypothesis of no difference between nonsmoking women of nonsmoking and

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smoking husbands. On the other hand, the studies should be replicated with better exposure information and more accurate death certificates. It appears that the other studies may have problems of design and/or analysis. Lung cancer risk, alleged to be twice as high in passive smokers as in nonsmokers not exposed to the smoke of their partner is hardly conceivable because of the absence of cell modifications in the tracheobronchial tract of passive smokers. Thus, the problem of passive smoking may be insignificant.

4. Gori G.B., Sidestream Smoke-Fact and Fiction - American Society of Heating, Refrigeration and Airconditioning Engineers, Inc., 1984.

- Proponents of non-smoker's rights to clean air have been anxious to reinforce their position with scientific evidence of health risks associated with passive exposure to tobacco smoke. Strong emotional pressures have influenced the design and interpretation of research efforts in this area. However, the combined evidence so far obtained does not support the contention that passive smoking under prevalent conditions is conducive to objectively measurable health risks.

- Clearly, whatever problems may be associated with passive smoking are likely to be small compared to other public health problems faced today. This, of course, is not to say smoking may not have dramatic adverse effects for certain narrow segments of the susceptible population, but in such cases intervention is easy and forthright. Studies will obviously continue to explore this field, but it is a foregone prediction that except for special circumstances and special matches of heavy exposure and susceptible populations the likelihood of finding future correlations of passive smoking exposure and significant public health problems is negligible.

5. Bock Fred G., Nonsmokers and Cigarette Smoke: A Modified Perception of Risk. Science, Vol. 215, January 8, 1982.

- To be sure, we do not know that any level of cigarette smoke is harmless. The model nonsmokers were exposed to levels exceeding the primary annual National Ambient Air Quality Standards. Small amounts of smoke are irritating to many nonsmokers and may physically impair some. Such effects by themselves are sufficient cause for concern about passive exposure to cigarette smoke. Risk of cancer and other diseases for which dose is important should not, however, be imputed from comparisons of nonsmokers with the least affected 2 percent of the smoking population.

6. Schievelbein H., Lung Carcinoma in Passive Smokers. Munch. Wschr. 123 (17) 1981.

- If the doubling of the relative risk of dying from lung cancer is actually attributable to passive smoking, there would be active here a dose which has up until now been regarded as harmless for human beings. According to unfavorable estimates, the constituents of the smoke of half of a filter cigarette, at the most, could be taken up by passive smoking. This dose is below, by a factor of 10 (or more), the threshold value hitherto regarded as harmful.

- According to Druckrey (), the lower the dose is, the longer the latency time is in chemical ccarcinogenesis. This means that lung cancer caused by passive smoking would appear, if at all, only at an age which, for the time being, remains unattainable for human beings. The same thing applies too, for the observation that the relative risk of passively smoking wives in the younger age-group is higher than in the older group, if control groups of the same age are used in comparison in each case. In regard to the latency time, what one would expect is the opposite of what was found.

- Finally, another marginal note on Hirayama's surprising finding "that passively smoking wives of farm workers carry a significantly higher risk of lung cancer (RR=4.6) than their urban fellow-sufferers". A statistical check of the numerical material presented shows that no such difference exists.

- On the basis of this evaluation, I have come to hold the view that since the Conference on Passive Smoking in the year 1977 in Munich, no really new knowledge has been acquired on the subject of passive smoking. It can be said that: passive smoking may mean an annoyance for heatlhy adults, but in all probability it is not connected with damage to health.

Wynder E.L., The Etiology, Epidemiology, and Prevention of Lung Cancer. Seminares in Respiratory medicine. Vol. 3, No.3 Jan. 1982.

- The fact that heavy cigar and pipe smokers who breathe in their own smoke most of the day have a relatively low risk of lung cancer and that bartenders and waiters who tend to work in smoke-filled rooms have not been reported to have a higher than expected rate of lung cancer does not suggest that passive inhalation of smoke constitutes a risk for the

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non-smoker. While side-stream smoke does contain the same types of tumorigenic agents contained in the mainstream smoke, quantitative studies on smoke components in a room suggest that the quantity, especially of particulate compounds, that could be inhaled by an individual would not suffice to provide a carcinogenic burden.

8. Gostomzky J.G., Disease Due to Passive Smoking? Munch. Med. Wschr. 124 (4), 1982.

- Preventive medicine requires as an operational base, data that should not only be significant in statistical tests, but should also be plausible.

  Even with statistical significance of the results, I do not find this hypothesis plausible. Other authors (Garkinkel, Lehnert) deplore the lack of plausibility also for Hirayama's idea on an increased risk of cancer in passive smokers because of the nondetectability of the dosage and the lack of a dosage-effect relationship.

9. Lee P.N. Passive Smoking. Fd. Chem. Tox. Vol. 20, 1982.

- Many studies indicate that nonsmokers are unlikely to inhale more than a very small amount of those components of tobacco smoke traditionally considered harmful. It was surprising, therefore, when a study carried out in the USA showed reduced airways function and studies from Japan and Greece showed an increased lung cancer incidence, in nonsmokers passively exposed to tobacco smoke in comparison with nonsmokers not so exposed. A review of the detail of these studies suggests that none provides conclusive evidence that passive smoking is seriously harmful, a view supported by a recent large study that was carried out in the USA and in which no significant relationship was found between passive smoking and lung cancer. More research is urgently needed, particularly to explore the influence of potentially confounding factors.

- For nicotine, Hogod et al. (1978) estimated it would take a passive smoker 50 hr to take in as much as would a smoker smoking one cigarette, an amount they regarded as negligible. Their results are broadly consistent with those of Hinds & First (1975) who estimated that nicotine concentratins in various public places in the USA ranged from the equivalent of one-thousandth of a filter cigarette per hour in a bus station waiting room up to almost one-hundredth in a cocktail lounge.